Supreme Court, U.S.

97 • 337 AUG 11 1997

OFFICE OF THE CLERK

No. 97-

IN THE

Supreme Court of the United States

OCTOBER TERM, 1997

GENENTECH, INC.,

Petitioner,

vs.

NOVO NORDISK A/S, NOVO NORDISK OF NORTH AMERICA, INC. and NOVO NORDISK PHARMACEUTICALS, INC.,

Respondents.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

PETITION FOR WRIT OF CERTIORARI

JOHN E. KIDD
Counsel of Record
LEORA BEN-AMI
JOSEPH FERRARO
PHILIP E. ROUX
ROGERS & WELLS
200 Park Avenue
New York, New York 10166
(212) 878-8000

Attorneys for Genentech, Inc.

90 pp

QUESTIONS PRESENTED

1. Did the Federal Circuit disregard settled law, including this Court's rulings and the text of 35 U.S.C. § 112, by ruling that a patent specification must state what is already known in the art?

   a. Did the Federal Circuit adopt an unworkably subjective test in ruling that information well known in the art may be used only to "supplement" a patent specification with "minor details?"

   b. Will the test adopted by the Federal Circuit panel call into question the validity of thousands of issued patents, lead to a substantial increase in the length of patent specifications (burdening the courts, the United States Patent and Trademark Office, and applicants), and diminish the ability of inventors to obtain meaningful patent coverage?

2. On appeal from a preliminary injunction, did the Federal Circuit have the authority, under 28 U.S.C. § 2106 or any other provision of law, to resolve disputed issues of fact and direct the entry of judgment, thereby denying plaintiff the opportunity to present a full record to a jury?

PARTIES TO THE PROCEEDING

Petitioner is Genentech, Inc. ("Genentech"). Roche Holdings Inc. ("Roche") owns approximately 66% of the issued shares of Genentech; however, Genentech remains an independent, publicly traded company and continues to operate entirely independently of Roche. Roche has an option to acquire the remaining shares of Genentech.

Respondents are Novo Nordisk, A/S., Novo Nordisk of North America, Inc. and Novo Nordisk Pharmaceuticals, Inc. (collectively "Novo").

TABLE OF CONTENTS

	Page
QUESTIONS PRESENTED	i
PARTIES TO THE PROCEEDING	ii
PETITION FOR A WRIT OF CERTIORARI	1
OPINIONS BELOW	1
JURISDICTION	1
STATUTORY PROVISIONS INVOLVED	1
STATEMENT OF THE CASE	2
REASONS FOR GRANTING THE PETITION	5
The Decision Fundamentally Alters The Law Of Enablement And Is Contrary To Precedent Of This Court And The Federal Circuit	5
The Federal Circuit Panel Erred In Ultimately Adjudicating And Dismissing Genentech's Claims On The Merits On An Appeal From A Preliminary Injunction	10
CONCLUSION	16

TABLE OF AUTHORITIES

Cases:	Page
Abraham Zion Corp. v. Lebow, 761 F.2d 93 (2d Cir. 1985)	14n.4
American Fed'n of Gov't Employees v. Colburn, 531 F.2d 314 (5th Cir. 1976)	14n.4
Barrett v. Roberts, 551 F.2d 662 (5th Cir. 1977)	14n.4
Brown & Williamson Tobacco Corp. v. Federal Trade Comm'n, 710 F.2d 1165 (6th Cir. 1983), *cert. denied* 465 U.S. 1100 (1984)	12
CES Publ'g Corp. v. St. Regis Publications, Inc., 531 F.2d 11 (2d Cir. 1975)	12
Chicago Observer, Inc. v. City of Chicago, 929 F.2d 325 (7th Cir. 1991)	12n.3
Chicago Observer, Inc. v. City of Chicago, 1990 WL 114189 at *2 (N.D. Ill. Aug. 1, 1990)	13n.3
Custom Accessories v. Jeffrey-Allan Indus., 807 F.2d 955 (Fed. Cir. 1986)	8
Dennison Mfg. Co. v. Panduit Corp., 475 U.S. 809 (1986)	11
Gellman v. State of Maryland, 538 F.2d 603 (4th Cir. 1976)	11, 14n.4
Genentech, Inc. v. Novo Nordisk, 108 F.3d 1361 (Fed. Cir. 1997)	4
Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367 (Fed. Cir. 1986)	5
In re Albrecht, 514 F.2d 1385 (CCPA 1975)	5, 6
In re Chilowsky, 229 F.2d 457 (CCPA 1956)	5
In re Howarth, 210 U.S.P.Q. 689 (CCPA 1981)	6

Cases: **Page**

In re Sureau, 373 F.2d 1002 (CCPA 1967) 6

In re Walter, 618 F.2d 758 (CCPA 1980)..... 8

Lawther v. Hamilton, 124 U.S. 1 (1888) 5

Libertarian Party of Indiana v. Packard, 741 F.2d 981 (7th Cir. 1984) 12

Lindemann Maschinenfabrik GMBH v. American Hoistand Derrick Co., 730 F.2d 1452 (Fed. Cir. 1984)..... 5

Litton Systems, Inc. v. Whirlpool Corp., 728 F.2d 1423 (Fed. Cir. 1984)..... 8

Markman v. Westview Instruments, Inc., 116 S. Ct. 1384 (1996)..... 13

Medtronics, Inc. v. Cardiac Pacemakers Inc., 721 F.2d 1563 (Fed. Cir. 1983) 8

Minerals Separation v. Hyde, 242 U.S. 261 (1916)... 5

Moses H. Cone Memorial Hospital v. Mercury Const. Corp., 460 U.S. 1 (1983)..... 13

Newell Cos., Inc. v. Kenney Mfg. Co., 864 F.2d 757 (Fed. Cir. 1988), *cert. denied*, 493 U.S. 814 (1989)..... 13

Novo Nordisk of North America, Inc. v. Genentech, Inc., 77 F.3d 1364 (Fed. Cir. 1996) 3

Para-Ordinance Mfg., Inc. v. SGS Importers Int'l., Inc., 73 F.3d 1085 (Fed. Cir. 1995), *cert. denied* 117 S. Ct. 80 (1996)..... 8

Paris v. United States Dept. of HUD, 713 F.2d 1341 (7th Cir. 1983) 14n.4

Penn v. San Juan Hospital, Inc., 528 F.2d 1181 (10th Cir. 1975) 14n.4

Cases:	**Page**
Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530 (Fed. Cir. 1983)	8
University of Texas v. Camenisch, 451 U.S. 390 (1981)	11, 14
Webster Loom Co. v. Higgins, 105 U.S. 580 (1881)	5
Wohlfahrt v. Memorial Med. Center, 658 F.2d 416 (5th Cir. 1981)	14n.4
Other Authorities:	
28 U.S.C. §2106	passim
28 U.S.C. §1254(1)	1
35 U.S.C. §112	i, 1, 4
Fed. R. Civ. P. 65(d)	12, 14
3 Donald Chisum, CHISUM ON PATENTS §7.03[2] (1997)	6

PETITION FOR A WRIT OF CERTIORARI

Petitioner Genentech respectfully prays that a writ of certiorari issue to review the Judgment and Opinion of the United States Court of Appeals for the Federal Circuit, dated March 13, 1997.

OPINIONS BELOW

The opinion and order of the court of appeals is reported at 108 F.3d 1361 (Fed. Cir. 1997) ("Decision")(Appendix A). The public version of The Findings of Fact and Conclusions of Law and The Order of Preliminary Injunction of the United States District Court, which were reversed on appeal, are reported at 935 F. Supp. 266 (S.D.N.Y. 1996) (Appendix B). The Order of the Court of Appeals for the Federal Circuit denying Genentech's petition for rehearing and suggestion for rehearing in banc is not reported (Appendix C).

JURISDICTION

The judgment of the United States Court of Appeals for the Federal Circuit was filed on March 13, 1997. A Petition for Rehearing was denied on May 12, 1997. The jurisdiction of this Court is invoked pursuant to Title 28, U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

The statutes involved in this Petition are 35 U.S.C. § 112 and 28 U.S.C. § 2106.

Section 112 sets out the required contents of a patent specification. It provides in relevant part:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make and use the same . . .

28 U.S.C. § 2106 provides in relevant part:

> The Supreme Court or any other court of appellate jurisdiction may affirm, modify, vacate, set aside or reverse any judgment, decree, or order of a court lawfully brought before it for review, and may remand the cause and direct the entry of such appropriate judgment, decree, or order, or require such further proceedings to be had as may be just under the circumstances.

STATEMENT OF THE CASE

This petition raises several questions of great importance to patent applicants and patent holders. Answers to these questions will determine the scope and content of future patent applications, as well as the validity and worth of patents already issued.

The technology at issue in this petition is directed to a recombinant DNA method for producing a human growth hormone product that is identical, or essentially identical, and functionally equivalent to the natural hormone. Human growth hormone ("hGH") is a protein secreted by the anterior pituitary gland. It has important metabolic effects, including stimulation of protein synthesis and cellular uptake of amino acids. The product is used to treat hypopituitary dwarfism in children.

Prior to Genentech's patented inventions, hGH for therapeutic use could be obtained only from the pituitary glands of human cadavers. The supply of pituitary-derived hGH was never sufficient to treat all children who required hGH, and, in any event, in 1985, the United States Food and Drug Administration ("FDA") withdrew marketing approval from pituitary-derived hGH because of its association with the deaths of several children. Later that same year, the FDA approved Genentech's recombinantly produced hGH product, Protropin®, which has been sold on the U.S. market continuously since then.

On November 30, 1994, in anticipation of receiving FDA approval for its hGH product, Norditropin®, Novo

commenced this action in the United States District Court for the Southern District of New York, alleging that various Genentech patents relating to hGH were invalid and not infringed. Genentech, in turn, asserted that Novo's Norditropin® infringed Genentech's patents. Novo received FDA approval for Norditropin® on May 9, 1995.

On May 12, 1995, Genentech moved, by order to show cause, for a temporary restraining order and a preliminary injunction prohibiting Novo from marketing and selling Norditropin® in the United States in violation of Genentech's United States Patent No. 4,601, 980 (the "'980 patent"). After conducting evidentiary hearings, the district court granted a preliminary injunction on June 28, 1995, but on February 26, 1996, the Court of Appeals for the Federal Circuit vacated the injunction, holding that the district court had applied an erroneous claim construction in determining that Genentech had established a likelihood of success on the merits of its claim for literal infringement. Specifically, the court held that literal language of Claim 2 of the '980 patent, read in light of the specification, was limited to a process known as "direct expression," and so did not cover Novo's process of making hGH. *See Novo Nordisk of North America, Inc.* v. *Genentech, Inc.*, 77 F.3d 1364, 1369 (Fed. Cir. 1996).

Meanwhile, during the pendency of the appeal, Genentech had obtained U.S. Patent 5,424,199 ("the '199 patent"). Genentech's '199 patent claims a method of recombinantly producing hGH by a process called "cleavable fusion expression." It is undisputed that Novo employs a "cleavable fusion expression" process to manufacture Norditropin®, its hGH product. On March 21, 1996, Genentech moved for a preliminary injunction based on the '199 patent.

The district court held evidentiary hearings on this motion from May 8, 1996 through May 23, 1996. On June 27, 1996, the district court issued a second preliminary injunction. (Appendix B). The district court based its decision, *inter alia*, upon a finding that Novo literally infringed the '199 patent and that Genentech would likely overcome Novo's defense

that the '199 patent was invalid for lack of an enabling disclosure under 35 U.S.C. § 112.

On March 13, 1997, a panel of the Federal Circuit vacated the second injunction and instructed the district court to dismiss Genentech's claim for infringement of the '199 patent. Specifically, the Federal Circuit panel concluded that the sole claim of the '199 patent was invalid under 35 U.S.C. § 112, holding that the '199 patent would not have enabled a person having ordinary skill in the art at the time of filing the patent application to employ the claimed "cleavable fusion" method to make hGH without undue experimentation. *See Genentech, Inc.* v. *Novo Nordisk*, 108 F.3d 1361 (Fed. Cir. 1997)(Appendix A). Moreover, instead of vacating the district court's grant of the preliminary injunction and remanding the case for trial, the panel invalidated the '199 patent and dismissed Genentech's claims on the merits.

Genentech sought rehearing on March 27, 1997. On May 12, 1997, the Federal Circuit denied the petition for rehearing and suggestion for rehearing in banc. (Appendix C).

As explained in more detail below, this Petition should be granted for two reasons.

First, the Decision fundamentally changes the basic law of enablement, erasing the well-settled bright line rule that a patent specification need not repeat information already well-known in the art, and adopting a new subjective rule that the specification must include all but "minor details." The new rule will affect virtually every new patent application, and will call into question the validity of thousands of issued patents.

Second, the decision fundamentally conflicts with the basic rules of appellate procedure. By transforming an interlocutory appeal into a final determination without notice or an opportunity to obtain and present new evidence, the decision violates this Court's precedent, the Federal Rules of Civil procedure and basic concepts of due process and fundamental

fairness and deprives Genentech of its right to a jury trial on enablement.

REASONS FOR GRANTING THE PETITION

The Decision Fundamentally Alters The Law Of Enablement And Is Contrary To Precedent Of This Court And The Federal Circuit

In order to obtain a valid patent, an applicant must disclose his invention in sufficient detail to enable the reader of the patent to practice the invention. The disclosure, however, is not directed to the layman, but to the person "skilled in the art to which [the invention] pertains." 35 U.S.C. § 112. Thus, by statute, every patent specification includes not only its explicit teachings, but also incorporates the knowledge and training of the hypothetical skilled artisan.

For more than a hundred years, the law of "enablement" has been settled, economical and clear; a patent applicant could enable his contribution to the art without repeating in the specification information which was already well-known. *See Lawther* v. *Hamilton*, 124 U.S. 1, 9-10 (1888) ("Every step of this process was already understood, although not connected in the manner pointed out in the patent...These several steps being well-known in the art when the patent was applied for, required no particular explanation...[E]very oil manufacturer in the country would understand [the patentee]. They would also understand that it might require additional care and skill to make the new process work successfully."); *See also*, *Minerals Separation* v. *Hyde*, 242 U.S. 261, 271 (1916); *Webster Loom Co.* v. *Higgins*, 105 U.S. 580, 586 (1881); *Hybritech Inc.* v. *Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well known in the art."); *Lindemann Maschinenfabrik GMBH* v. *American Hoist and Derrick Co.*, 730 F.2d 1452, 1463 (Fed. Cir. 1984)(same); *In re Chilowsky*, 229 F.2d 457, 460 (CCPA 1956)("It is well settled that the disclosure of an application embraces not only what is expressly set forth in words or drawings, but what would be understood by persons skilled in the art"); *In re Albrecht*, 514

F.2d 1385, 1389 (CCPA 1975) (court permitted applicant to rely upon disclosure of earlier patent to supply information on how to make specific starting materials); *In re Sureau*, 373 F.2d 1002 (CCPA 1967) (applicant could rely on information in prior art even though specification did not expressly disclose details of process); 3 Donald Chisum, CHISUM ON PATENTS § 7.03[2] (1997). Moreover, the skilled person's knowledge was deemed to include not only information he would be expected to know, but also information he could reasonably be expected to locate. *In re Howarth*, 210 U.S.P.Q. 689, 692 (CCPA 1981) (information in the prior art could be used for purposes of enablement when a person "skilled in the art...reasonably would be expected to check the source which the applicant relies upon to complete his disclosure and would be able the locate the information with no more than reasonable diligence.")

Thus, until the panel's Decision, the courts and the PTO uniformly measured enablement by using a fact-based bright-line test: if information was known to those skilled in the art, it could and should be omitted. This was the test which the PTO applied in examining the '199 patent application and in issuing the '199 patent, and the test which the district court used in ruling that Genentech was likely to succeed on its claims.[1]

---

[1] Indeed, it is undisputed that during the prosecution of the '199 patent before the PTO, the patent examiner initially rejected the '199 patent application for lack of enablement on the same ground that the Federal Circuit held the '199 patent invalid: because the disclosure of one enzyme (trypsin) and a cleavable sequence (arg-arg, lys-lys) did not enable a generic claim for the cleavable fusion process. Responding to this objection, Genentech provided ample documentary evidence of the state of the art, and demonstrated that the prior knowledge in the art, together with the teachings in the specification, would enable the skilled worker to practice the generic claims of the invention. The Examiner, applying the standards for enablement which existed prior to the panel's decision in this case, agreed and granted the generic claims (Appendix B at ¶ 43). The district court applied that same standard for enablement at the preliminary injunction hearing and similarly found a likelihood of success on enablement. *Id.* at ¶ 42.

The Decision discards this objective standard, characterizing the former rule as "merely a rule of supplementation" which permits only "the omission of minor details" (Appendix A at 8-9). Specifically, the Decision's new test for enablement is as follows:

> It is true, as Genentech argues, that a specification need not disclose what is well known in the art. [citations omitted]. However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of *minor details* does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of *any specific starting material or of any of the conditions under which a process can be carried out*, undue experimentation is required; there is a failure to meet the enablement requirement that *cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art*. It is the specification, not the knowledge of one skilled in the art, that must supply the *novel aspects* of the invention in order to constitute adequate enablement.

Id. (emphasis added)

Genentech is unaware of any decision by this Court or any other decision by the Federal Circuit or its predecessor courts which places limits on a patent applicant's ability to rely upon knowledge available to those of ordinary skill in the art for purposes of proving enablement. By doing so, the panel's Decision drastically departs from settled law and contradicts Supreme Court and Federal Circuit precedent.

Moreover, in place of the former objective standard, the panel's Decision substitutes three vague and elusive concepts: "novel aspects," "[mere] supplementation," and "minor details." Thus, the panel's Decision demands that the specification itself, without reference to the art, must supply the "novel aspects" of an invention. *Id.* There is no law, and the Decision

cites none, supporting the proposition that the state of the art cannot supply the novel aspects (whatever that phrase may mean) of a claimed invention. Section 112 states:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same....

Section 112 suggests no "novel aspects" test, but views the invention as a whole, considering the specification in conjunction with the art. The patentee must enable the claimed invention, viewed as a whole; dividing the invention into "novel" and "non-novel" aspects for purposes of testing enablement is unprecedented. While in the past, misguided attempts were made to analyze issues of obviousness by looking to the invention's "point of novelty" rather than to the invention as a whole, that test proved unworkable and was utterly rejected by the Federal Circuit. *See Para-Ordinance Mfg., Inc.* v. *SGS Importers Int'l., Inc.*, 73 F.3d 1085 (Fed. Cir. 1995), *cert. denied* 117 S. Ct. 80 (1996) (no "heart of the invention" in an obviousness determination); *Litton Systems, Inc.* v. *Whirlpool Corp.*, 728 F.2d 1423, 1444 (Fed. Cir. 1984) ("This 'point of novelty' approach applies only to a determination of infringement...This court has avoided the point of novelty approach in other contexts."); *Medtronics, Inc.* v. *Cardiac Pacemakers Inc.*, 721 F.2d 1563, 1567 (Fed. Cir. 1983) ("Though applicable elsewhere, e.g., in determining infringement under the doctrine of equivalents, there is no legally recognized 'essence' of the invention applicable in determining validity."); *Custom Accessories* v. *Jeffrey-Allan Indus.*, 807 F.2d 955, 959 (Fed. Cir. 1986); *Stratoflex, Inc.* v. *Aeroquip Corp.*, 713 F.2d 1530, 1540 (Fed. Cir. 1983); *In re Walter*, 618 F.2d 758, 766 (CCPA 1980). The "novel aspects" test for enablement should also be rejected. Moreover, by dividing out the "novel aspects" of an invention and stating that those aspects must be explicit in the specification, the Federal Circuit panel has rewritten the law on enablement and applied

this new law retroactively to a patent application filed in 1979, when no such "novel aspects" standard existed.

Similarly, the Decision provides no guidelines to measure the degree of "supplementation" allowed, or to measure when an "omission" rises above the subjective level of "minor details". In the present case, the panel's Decision held that standard reaction conditions for known enzymes had to be explicitly disclosed in patent specifications.[2] Yet the evidence submitted on the preliminary injunction hearing showed that such reaction conditions were already well-known and were readily available from standard reference texts which workers in the biotechnology field would routinely consult (Appendix B at ¶¶ 51-55, 63-69). The Decision offers no guidance as to why such an enzyme reaction condition is not merely "supplementation" or a "minor detail." This new, subjective standard will disserve the judicial system and patentees. Patents granted many years ago under the old standard can now be invalidated by a finding that the specification omitted something which was known to the prior art but was not merely a supplementary "minor detail."

The panel's Decision will have effects well beyond this case. The Decision was published and can be cited as precedent, but its failure to provide any guidance to the lower courts or the PTO to determine what constitutes a "minor detail" or a "novel aspect" of an invention will irreparably harm the patent system by promoting inconsistent district court decisions and unreliable PTO actions. Many hundreds of thousands of patent applications were drafted, filed, examined and allowed under the old standard and remain unexpired. Those patents are the property of a multitude of corporations and inventors. Retroactive application of a "mere supplementation" with "minor details" test will call into question the

---

[2] The Decision states definitively and without qualification that a failure to disclose a starting material or process condition in the patent application leads to the unwavering conclusion that the patent is not enabled because of undue experimentation. (Appendix A at 8).

validity of these patents and work havoc with this major component of U.S. intellectual property. Prospective application of such a test, which requires the specification to repeat prior art in the specification will result in patent specifications of enormous length, thus increasing the burden on inventors, corporations, the PTO, and courts.

Because the Decision has changed the basic rules for enablement and overruled clear precedent, this Petition should be granted.

The Federal Circuit Panel Erred In Ultimately Adjudicating And Dismissing Genentech's Claims On The Merits On An Appeal From A Preliminary Injunction

In vacating the preliminary injunction, the panel did more than change the test for enablement. It also changed the function of an appellate court. The panel treated the preliminary injunction record as though it were a full record, made findings of fact as though it were a trial court, held that the '199 patent was invalid, and dismissed Genentech's claims on the merits. In its decision, the panel stated: "since we are able to review the record and read the specification, there is no reason why we should limit our decision here to reversing the grant of the preliminary injunction." (Appendix A at 13). In fact, there are compelling reasons why the Federal Circuit panel should not have used an incomplete record to support a final decision on the merits.

Under the banner of judicial economy, the Federal Circuit panel conducted a trial at the appellate level of disputed issues of fact and deprived Genentech of due process and of its right to a trial by jury. The Federal Circuit panel weighed evidence, examined the record outside the pleadings and made factual determinations without paying any deference to the contrary and detailed findings made by the district court. More importantly, the Federal Circuit panel denied Genentech its opportunity to present a complete trial record.

This Court has warned that it is inappropriate for a court to reach the merits of the case at the preliminary injunction stage, given the expedited nature of the proceeding and the limited nature of the record. As the Court stated in *University of Texas* v. *Camenisch*, 451 U.S. 390, 395 (1981):

> [A] preliminary injunction is customarily granted on the basis of procedures that are less formal and evidence that is less complete than in a trial on the merits. A party thus is not required to prove his case in full at a preliminary-injunction hearing, *Progress Development Corp.* v. *Mitchell*, 286 F.2d 222 (C.A.7 1961), and the findings of fact and conclusions of law made by a court granting a preliminary injunction are not binding at trial on the merits, *Industrial Bank of Washington* v. *Tobriner*, 132 U.S. App. D.C. 51, 54, 405 F.2d 1321, 1324 (1968); *Hamilton Watch Co.* v. *Benrus Watch Co.*, 206 F.2d 738, 742 (C.A.2 1953). In light of these considerations, it is generally inappropriate for a federal court at the preliminary-injunction stage to give a final judgment on the merits. *E.g.*, *Brown* v. *Chote*, *supra*; *Gellman* v. *Maryland*, 538 F.2d 603 (C.A.4 1976); *Santiago* v. *Corporacion de Renovacion Urbana y Vivienda de Puerto Rico*, 453 F.2d 794 (C.A.1 1972).

Indeed, in *Camenisch*, this Court cited with approval *Gellman* v. *State of Maryland*, 538 F.2d 603, 606 (4th Cir. 1976), which described the trial court's decision to dismiss at the close of a preliminary injunction hearing as "perilously close to a violation of due process."

The Decision states that enablement is a question of law "based upon several underlying factual inquiries" (Appendix A at 6). That the ultimate conclusion is one of law, however, does not permit the appellate court to ignore the underlying findings made by the district court, or to substitute its own findings on an incomplete record. Indeed, in *Dennison Mfg. Co.* v. *Panduit Corp.*, 475 U.S. 809, 811 (1986), this Court

reminded the Federal Circuit that even if Rule 52(a) did not apply to "the ultimate question of obviousness," the "subsidiary determinations of the District Court, at the least, ought to be subject to the Rule."

In suggesting that the parties agreed at oral argument that the enablement issue had been "thoroughly ventilated," the Decision is neither accurate nor fair, but even if the issue had been "thoroughly ventilated" (which it could not have been on an incomplete record), the Federal Circuit panel was not entitled to make factual findings which would dispose of Genentech's claims on the merits. Neither 28 U.S.C. § 2106 (the only authority relied on by the Federal Circuit), nor Rule 65(a), Fed. R. Civ. P., nor any other provision of law gave the Federal Circuit the authority to do so.

While 28 U.S.C. § 2106, in very general terms, gives an appellate court the power to direct the entry of an appropriate judgment or order to give effect to its decision, it does not change the essential function of an appellate court nor turn it into a trial court. Appellate courts have properly directed the entry of judgment in cases where the facts had already been tried, where there were no issues of fact, or where the case had become moot while the appeal was pending. *See e.g. Brown & Williamson Tobacco Corp.* v. *Federal Trade Comm'n*, 710 F.2d 1165, 1173 (6th Cir. 1983), *cert. denied* 465 U.S. 1100 (1984); *CES Publ'g Corp.* v. *St. Regis Publications, Inc.*, 531 F.2d 11 (2d Cir. 1975); *Libertarian Party of Indiana* v. *Packard*, 741 F.2d 981 (7th Cir. 1984). Genentech has discovered no case, nor did Novo cite any below, in which an appellate court has relied on 28 U.S.C. § 2106 to make fact findings and enter judgment on the merits after a preliminary injunction hearing.[3] In an ardent dissent, joined

---

[3] *Chicago Observer, Inc. v. City of Chicago*, 929 F.2d 325, 329 (7th Cir. 1991), relied on by the panel, adds nothing to the court's authority. In that case, the parties agreed to submit the controversy on papers. As the district court stated:

> At the hearing on July 24, 1990, the parties were given an opportunity to present additional evidence and to orally argue

(Footnote continued)

by Chief Justice Burger and Justice O'Connor, then Justice Rehnquist reminded this Court that the reach of § 2106 was not unlimited and should be reserved for extraordinary circumstances. Justice Rehnquist went on to state:

> This statute does not grant the courts of appeals authority to constitute themselves as trial courts. Section 4 of the Arbitration Act gives the Hospital a right to a jury trial. (citations omitted) By deciding that there were no disputed issues of fact, the Court of Appeals seems to have decided a motion for summary judgment that was not before it. This is the kind of issue that district court judges decide every day in the ordinary course of business. It is not the kind of issue that courts of appeals determine.

Moses H. Cone Memorial Hospital v. *Mercury Const. Corp.*, 460 U.S. 1, 35 (1983) (Rehnquist, J., dissenting). In the instant case, the Federal Circuit panel did not simply decide that there were no disputed issues of fact. Here, the appellate court actually decided disputed material facts and disposed of an issue that has traditionally been reserved for the jury. It is well established that the issue of enablement is a question to be tried to the jury. *See, e.g., Newell Cos., Inc.* v. *Kenney Mfg. Co.*, 864 F.2d 757, 775 (Fed. Cir. 1988), *cert. denied* 493 U.S. 814 (1989). *See also, Markman* v. *Westview Instruments, Inc.*, 116 S. Ct. 1384 (1996). Here, Genentech demanded a jury, and has not waived its jury right. Thus, the court could properly deprive Genentech of its right to a trial by jury only by finding that there were no facts in dispute, not by finding and deciding them.

> their positions. Both parties declined this opportunity on the ground that the issues were fully presented, both factually and legally, in the written materials previously submitted to the court.

Chicago Observer, Inc. v. City of Chicago, 1990 WL 114189, at *2 (N.D. Ill. Aug. 1, 1990).

Nor could the Federal Circuit panel properly decide the merits by looking to Rule 65(a), Fed. R. Civ. P., which allows the trial court to consolidate the trial on the merits with the preliminary injunction hearing. This Court and the Courts of Appeals[4] have uniformly held that the court may not invoke this power retroactively, as the Federal Circuit panel did here. Instead, this Court held in *Camenisch*:

> Before such an order may issue, however, the courts have commonly required that "the parties should normally receive clear and unambiguous notice [of the court's intent to consolidate the trial and the hearing] either before the hearing commences or at a time which will still afford the parties a full opportunity to present their respective cases." *Pughsley v. 3750 Lake Shore Drive Cooperative Bldg.*, 463 F.2d 1055, 1057 (C.A.7 1972); *Nationwide Amusements, Inc. v. Nattin*, 452 F.2d 651 (C.A.4 1971).

Camenisch, 451 U.S. at 395.

No such notice was given in the present case. Indeed, it is undisputed that the trial judge in this case repeatedly emphasized the limited nature of the hearing, and confirmed that it was not a full trial. Moreover, there has been no discovery yet, except for discovery on other patents carried over from an earlier International Trade Commission proceeding. If a trial court cannot accelerate the trial on the merits from an incomplete record unless it gives the parties notice and an opportunity to present evidence, then an appellate court should never

---

[4] *E.g.*, *University of Texas v. Camenish*, 451 U.S. 390 (1981); *Abraham Zion Corp. v. Lebow*, 761 F.2d 93 (2d Cir. 1985); *Paris v. United States Dep't of HUD*, 713 F.2d 1341 (7th Cir. 1983); *Wohlfahrt v. Memorial Med. Center*, 658 F.2d 416 (5th Cir. 1981); *Barrett v. Roberts*, 551 F.2d 662 (5th Cir. 1977); *Gellman v. State of Maryland*, 538 F.2d 603 (4th Cir. 1976); *American Fed'n of Gov't Employees v. Colburn*, 531 F.2d 314 (5th Cir. 1976); *Penn v. San Juan Hospital, Inc.*, 528 F.2d 1181 (10th Cir. 1975).

be able to do so, since an appellate court cannot give the parties such an opportunity.

Section 2106 allows an appellate court to "direct the entry of such appropriate judgment...as may be just under the circumstances." Genentech urges this Court to review the record surrounding the Federal Circuit's panel's dismissal of this case and invalidation of the '199 patent, taking into consideration at least the following: (1) the panel reversed the preliminary injunction by fundamentally altering the law of enablement and disregarding this Court's precedent; (2) the panel ignored the findings of fact of the district court and decided issues of material fact based on an incomplete record of an expedited proceeding; (3) the panel was clearly informed by Genentech that the record was not complete; and (4) there was no notice to Genentech that the panel would make a final determination nor an opportunity for Genentech to obtain and present further evidence. In light of these factors, Genentech respectfully submits that the panel's adjudication was not "just under the circumstances."

CONCLUSION

This dispute presents an exceptional case in which a writ of certiorari should be granted. The Federal Circuit panel's drastic departure from this Court's precedent on the law of patent enablement discards a clear test and adopts a vague and subjective one, leaving the district courts, the PTO, patent attorneys and inventors in a state of uncertainty and confusion. Moreover, this case provides the Court with a rare opportunity to correct an abuse of appellate authority by the Federal Circuit, and in so doing, to confirm the appropriate level of deference owing to the factual findings of district courts.

Dated: August 11, 1997

Respectfully submitted,

JOHN E. KIDD
Counsel of Record
LEORA BEN-AMI
JOSEPH FERRARO
PHILIP E. ROUX

ROGERS & WELLS
200 Park Avenue
New York, New York 10166
(212) 878-8000

Attorneys for Genentech, Inc.

APPENDIX A

Appendix A

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

96-1440

GENENTECH, INC.,

Plaintiff-Appellee,

v.

NOVO NORDISK A/S, NOVO NORDISK OF NORTH AMERICA, INC., and NOVO NORDISK PHARMACEUTICALS, INC.,

Defendants-Appellants.

DECIDED: March 13, 1997

Before ARCHER, *Chief Judge*, LOURIE, and BRYSON, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Novo Nordisk A/S, Novo Nordisk of North America, Inc., and Novo Nordisk Pharmaceuticals, Inc. (collectively "Novo") appeal from the order of the United States District Court for the Southern District of New York, issuing a preliminary injunction in favor of Genentech, Inc., enjoining Novo from importing, marketing, using, selling, offering for sale or distributing its Norditropin®-brand recombinant human growth hormone (hGH) product. *Genentech, Inc. v. Novo Nordisk A/S*, 935 F. Supp. 260 (S.D.N.Y. 1996). Because the district court's conclusion that Genentech had demonstrated a likelihood of success on the merits was based on an error of law and because its remaining findings were premised on this error, we vacate the injunction.

BACKGROUND

This consolidated patent infringement action was first brought in the United States District Court for the Southern District of New York on November 30, 1994. On May 12, 1995, Genentech moved for a preliminary injunction under U.S. Patent 4,601,980 to prevent Novo from importing, marketing, using, selling, offering for sale or distributing in the United States its Norditropin®-brand recombinant hGH product. The district court granted Genentech's motion and issued an injunction. *Novo Nordisk of North Am., Inc. v. Genentech, Inc.*, No. 94 Civ. 8634 (CBM), 1995 U.S. Dist. LEXIS 12588, 1995 WL 512171 (S.D.N.Y. Aug. 28, 1995).

On appeal this court vacated the injunction. *Novo Nordisk of North Am., Inc. v. Genentech, Inc.*, 77 F.3d 1364, 37 USPQ2d 1773 (Fed. Cir. 1996). We held that the district court clearly erred in finding that Genentech established a likelihood of proving infringement of the '980 patent because that finding was based on an improper construction of claim 2 of the patent. Based upon the specification and prosecution history, we concluded that because the claim used the phrase "human growth hormone unaccompanied by . . . other extraneous protein," it was limited to processes for directly expressing either hGH or met-hGH. *Id.* at 1371, 37 USPQ2d at 1779. Because the parties agreed that Novo did not use direct expression to produce these proteins, we concluded that Novo did not infringe the patent. *Id.*

Upon returning to the district court, Genentech asserted its newly issued U.S. Patent 5,424,199. The '199 patent has the same specification as the '980 patent and contains a single claim directed to:

> [a] method of producing a protein consisting essentially of amino acids 1-191 of human growth hormone comprising:
>
> (a) expressing in a transformant bacterium, DNA coding for a human growth hormone conjugate protein, which conjugate protein consists

> essentially of amino acids 1-191 of human growth hormone as set forth in combined Figs. 1 and 3 unaccompanied by the leader sequence of human growth hormone or other extraneous protein bound thereto and an additional amino acid sequence which is specifically cleavable by enzymatic action, and
>
> (b) cleaving extracellularly said conjugate protein by enzymatic action to produce said protein consisting essentially of amino acids 1-191 of human growth hormone.

This claim differs from the claim adjudicated in the prior case in reciting that the encoded protein has an additional amino acid sequence and includes the step of cleaving this conjugate protein. This process of expressing a DNA encoding a conjugate protein and using an enzyme to cleave off an undesired portion of that protein is generally known as cleavable fusion expression. The parties agree that Novo uses cleavable fusion expression to produce hGH. *Id.*

On June 27, 1996, after conducting a twelve-day evidentiary hearing, the district court again issued a preliminary injunction, this time based upon the '199 patent, enjoining Novo from importing, marketing, using, selling, offering for sale, or distributing in the United States its Norditropin®-brand recombinant hGH product. *Genentech v. Novo Nordisk A/S*, 935 F. Supp. 260 (S.D.N.Y. 1996). The district court based its decision upon, *inter alia*, a finding that Genentech would likely overcome Novo's defense that the '199 patent was invalid for lack of an enabling disclosure under 35 U.S.C. § 112, ¶ 1 (1994).

Novo appeals to this court, challenging the grant of the preliminary injunction.[1] We have jurisdiction pursuant to 28 U.S.C. § 1292(c) (1994).

---

[1] On July 3, Novo moved for an emergency stay of the injunction pending disposition of this appeal. On August 1, we denied Novo's motion and

(Footnote continued)

DISCUSSION

The grant or denial of a preliminary injunction pursuant to 35 U.S.C. § 283 is within the discretion of a district court. *We Care, Inc. v. Ultra-Mark Int'l Corp.*, 930 F.2d 1567, 1570, 18 USPQ2d 1562, 1564 (Fed. Cir. 1991). Accordingly, a trial court's decision granting a preliminary injunction will be overturned on appeal only upon a showing that the court abused its discretion. *Joy Techs., Inc. v. Flakt, Inc.*, 6 F.3d 770, 772, 28 USPQ2d 1378, 1380 (Fed. Cir. 1993). Such an abuse of discretion may be established by showing that the court made a clear error of judgment in weighing relevant factors or exercised its discretion based upon an error of law or clearly erroneous factual findings. *Id.*

As the moving party, Genentech had to establish its right to a preliminary injunction in light of four factors: (1) a reasonable likelihood of success on the merits; (2) irreparable harm if the injunction were not granted; (3) the balance of the hardships; and (4) the impact of the injunction on the public interest. *Nutrition 21 v. United States*, 930 F.2d 867, 869, 18 USPQ2d 1347, 1348-49 (Fed. Cir. 1991); *Hybritech Inc. v. Abbott Labs.*, 849 F.2d 1446, 1451, 7 USPQ2d 1191, 1195 (Fed. Cir. 1988).

A. *Likelihood of Success on the Merits*

In order to demonstrate that it has a likelihood of success, Genentech must show that, in light of the presumptions and burdens that will inhere at trial on the merits, (1) it will likely prove that Novo infringes the '199 patent and (2) its infringement claim will likely withstand Novo's challenges to the validity and enforceability of the '199 patent. *See New England Braiding Co. v. A.W. Chesterton Co.*, 970 F.2d 878,

---

reinstated the injunction. However, after having heard oral argument in this case, we reconsidered the motion and reinstated the stay of the injunction.

882-83, 23 USPQ2d 1622, 1625-26 (Fed. Cir. 1992).[2] In other words, if Novo raises a "substantial question" concerning validity, enforceability, or infringement (*i.e.*, asserts a defense that Genentech cannot show "lacks substantial merit") the preliminary injunction should not issue. *Id.* More specifically, with regard to Novo's validity defenses, the question on appeal is whether there is substantial merit to Novo's assertion that the '199 patent claim fails to meet the requirements of 35 U.S.C. § 112, ¶ 1 (1994).

Novo argues that the district court's findings regarding validity under § 112, ¶ 1, are clearly erroneous because it presented clear and convincing evidence that the patent specification would not have enabled a person of ordinary skill in the art to practice the claimed invention without undue experimentation. Novo also argues that the specification fails to contain a written description of the claimed invention. Regarding enablement, Novo argues that the patent is invalid because it does not contain sufficient detail concerning the practice of the claimed method. Novo argues that the mere generic statement of the possibility of cleavable fusion expression, along with the DNA sequence encoding hGH, a single enzyme (trypsin) for cleaving undisclosed conjugate proteins, and a statement of that enzyme's cleavage sites as being potential amino acid extensions conjugated to hGH is not an enabling disclosure commensurate in scope with the claim. Genentech responds that all of the district court's factual findings regarding enablement are supported by the record. More specifically, Genentech argues that those skilled in the art of recombinant protein expression and purification at the time of filing, July 5, 1979, would have been able to use

---

[2] A patent is presumed valid, 35 U.S.C. § 282 (1994), and a party challenging validity must prove invalidity by clear and convincing evidence. "However, the presumption does not relieve a patentee who moves for preliminary injunction from carrying the normal burden of demonstrating that it will likely succeed on all disputed liability issues at trial, even when the issue concerns the patent's validity." *New England Braiding*, 970 F.2d at 882, 23 USPQ2d at 1625 (citing *Nutrition 21*, 930 F.2d at 869, 18 USPQ2d at 1349).

cleavable fusion expression to produce hGH without undue experimentation by using the teachings of the specification along with methods and tools well known in the art. We conclude that Novo has raised more than a substantial question concerning the validity of the '199 patent. In fact, it has shown that the patent is invalid.

Section § 112, ¶ 1, provides, in relevant part that:

> [t]he specification shall contain a written description of the invention, and the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same. . . .

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) ("[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."). Whether making and using the invention would have required undue experimentation, and thus whether the disclosure is enabling, is a legal conclusion based upon several underlying factual inquiries. *See In re Wands*, 858 F.2d 731, 735, 736-37, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988).

The question before us is whether the specification would have enabled a person having ordinary skill in the art at the time of filing to use cleavable fusion expression to make hGH without undue experimentation. There is no dispute that the portion of the specification chiefly relied upon by Genentech and by the district court, column 7, lines 29-59, does not describe in any detail whatsoever how to make hGH using cleavable fusion expression. For example, no reaction conditions for the steps needed to produce hGH are provided; no

description of any specific cleavable conjugate protein appears. The relevant portion of the specification merely describes three (or perhaps four) applications for which cleavable fusion expression is *generally* well-suited and then names an enzyme that might be used as a cleavage agent (trypsin), along with sites at which it cleaves ("arg-arg or lys-lys, etc.").[3] Thus, the specification does not describe a specific material to be cleaved or any reaction conditions under which cleavable fusion expression would work.

Notwithstanding this limited disclosure, Genentech argues (and the district court found) that those of ordinary skill in the art would have been able to practice the claimed invention without undue experimentation. Essentially, Genentech's argument is that the knowledge of one skilled in the art was sufficient to provide all of the missing information and, more specifically, that the disclosure of a DNA encoding hGH, when combined with prior art cleavable fusion expression techniques applied to non-human proteins, would enable the practice of the claimed method. In support of this argument, Genentech points to the testimony of Dr. Ravetch, who testified as to the knowledge of one skilled in the art, to the extensive description of enzymes in the reference textbook *Methods in Enzymology*, and to the specification's explicit reference to British Patent 2008123-A, which more fully details the potential use of trypsin in cleavable fusion expression.

In response to these arguments, Novo asserts that at the time of filing, trypsin and other like enzymes were used only to digest proteins, not to specifically and precisely cleave conjugate proteins to yield intact, useful proteins, and that the British patent explicitly indicates that trypsin would not be

---

[3] At column 7, lines 52-58, the specification states: "At least in the latter three applications [of the four applications that are disclosed], the synthetic adaptor molecular [sic] employed to complete the coding sequence of the mRNA transcript can additionally incorporate codons for amino acid sequences specifically cleavable, as by enzymatic action. For example, trypsin will cleave specifically at arg-arg or lys-lys, etc."

useful for the cleavable fusion expression of arginine-containing proteins such as hGH. Novo further argues that neither the specification nor the references cited by Genentech suggest a single amino acid sequence, out of the virtually infinite range of possibilities, that would yield hGH in a useful form when cleaved from the conjugate protein.

We agree with Novo. Genentech's arguments, focused almost exclusively on the level of skill in the art, ignore the essence of the enablement requirement. Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. That requirement has not been met in this specification with respect to the cleavable fusion expression of hGH.

It is true, as Genentech argues, that a specification need not disclose what is well known in the art. *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an

invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

The specification indicates that it purports to solve a problem. That problem is summarized at column 3, line 65, through column 4, line 8:

> [A] need has existed for new methods of producing hGH and other polypeptide products in quantity and that need has been particularly acute in the case of polypeptides too large to admit to organic synthesis or, for that matter, microbial expression from entirely synthetic genes. Expression of mammalian hormones from mRNA transcripts . . . has permitted only microbial production of bio-inactive conjugates from which the desired hormone could not practically be cleaved.

The problem thus was the difficulty of obtaining hGH from a precursor containing added protein material. This problem was solved by the description of a method of obtaining hGH unaccompanied by a leader sequence or other extraneous proteins, as claimed in the '980 patent. However, the specification for the '199 patent, which is the same as the specification for the '980 patent, does not provide a specific enabling disclosure concerning what the new claim recites, *viz.*, obtaining hGH by cleaving an hGH-containing conjugate protein. That was the problem avoided by the invention claimed in the '980 patent. The present specification contains no more disclosure than the '980 specification, but this patent now purports to claim the unresolved problem that the '980 patent overcame. Genentech is attempting to bootstrap a vague statement of a problem into an enabling disclosure sufficient to dominate someone else's solution of the problem. This it cannot do.

Genentech's arguments in favor of enablement are unavailing. While Genentech's witness, Dr. Ravetch, did state that it would have been possible for a skilled artisan to create a DNA sequence coding for arg-arg-hGH or lys-lys-hGH, he

did not discuss the experimentation needed for the creation of DNA coding for more extensive sequences, such as those that have proved necessary to the production of hGH via cleavable fusion expression. Likewise, the description of a wide range of enzymes in *Methods in Enzymology*, by itself, does not render routine the determination of an enzyme-conjugate protein combination. Rather, as Novo argues and the record reflects, various combinations of conjugate protein sequences, cleaving enzymes, and reaction conditions needed to be studied to establish a process for producing hGH in useful form. Finally, the British patent cited in the specification actually works against Genentech's position by explicitly teaching that trypsin would not work well to produce hGH. The specification does not even acknowledge any of the known difficulties associated with using trypsin on an hGH conjugate protein. This specification is so lacking with respect to the limitation of paragraph (b) of claim 1 that providing testimony regarding the skill in the art has been an exercise in futility.

The limited testimony regarding the knowledge of one skilled in the art offered by Genentech at the preliminary injunction hearing, and relied upon by the district court, is further undermined by the fact that no one had been able to produce *any* human protein via cleavable fusion expression as of the application date. If, as Genentech argues, one skilled in the art, armed only with what the patent specification discloses (a DNA sequence encoding a human protein, in this case, hGH, and a single example of an enzyme and its cleavage site), could have used cleavable fusion expression to make a human protein without undue experimentation, it is remarkable that this method was not used to make any human protein for nearly a year, *see* Shine *et al.*, 285 Nature 456 (June 1980), or to make hGH for five years. *See* Belagaje *et al.*, 3 DNA 120 (1984). Certainly, DNAs encoding desirable human proteins were known at the time of filing (*e.g.*, insulin, described in the British patent), and a great many researchers were attempting to produce human proteins using recombinant DNA technology. This failure of skilled scientists, who were supplied with the teachings that Genentech asserts were sufficient and who were clearly motivated to produce human

proteins, indicates that producing hGH via cleavable fusion expression was not then within the skill of the art. The contrary testimony offered by Genentech's witnesses, who hypothesized about the skill of the art more than fifteen years earlier, does not demonstrate the incorrectness of Novo's arguments. *See In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991) ("[A]n expert's opinion on the ultimate legal issue [of enablement] must be supported by something more than a conclusory statement.").

Moreover, it stands to reason that if the disclosure of a useful conjugate protein and the method for its cleavage were so clearly within the skill of the art, it would have been expressly disclosed in the specification, and in the usual detail. Patent draftsmen are not loath to provide actual or constructive examples, with details, concerning how to make what they wish to claim. In addition, as indicated above, the specification of this patent was clearly drafted to claim the invention of obtaining hGH *unaccompanied by* extraneous protein, the cleavage of which was identified by the specification as a problem in this field. Genentech's inventors knew how to enable that which they had invented. These facts underline the inadequacy of the specification in enabling that which it provided only a means to avoid.

The record does not support the district court's implicit finding that the disclosure of trypsin and its cleavage site enables the production of any conjugate protein from which hGH can practically be cleaved and thus produced in useful form; the record indicates that determination of these features required further undue experimentation. None of the expert testimony relied upon by Genentech or by the district court suggests otherwise.[4] Where, as here, the claimed invention is

---

[4] Novo's witness, Dr. Villa-Komaroff, merely stated on cross- examination that, assuming arg-arg-hGH was initially produced and successfully extracted from the transformed cell, that "[u]nder the best condition, approximately five percent of the time there will be in the [post-digestion] mix [hGH]." This statement, characterized by Genentech as an admission, was made in the limited context of partial trypsin digests of isolated

(Footnote continued)

the application of an unpredictable technology in the early stages of development, an enabling description in the specification must provide those skilled in the art with a specific and useful teaching. Genentech has not shown that the '199 patent provides that teaching.

Under the circumstances, we are compelled to conclude that the district court made an error of law in ruling that Genentech showed a likelihood of success on enablement. *See In re Epstein*, 32 F.3d 1559, 1568, 31 USPQ2d 1817, 1823 (Fed. Cir. 1994) ("[E]nablement is a question of law . . . which may involve subsidiary questions of fact."). Furthermore, since we are able to review the record and to read the specification, there is no reason why we should limit our decision here to reversing the grant of the preliminary injunction. Rather, because the parties agreed at oral argument that the enablement issue had been thoroughly ventilated by the extensive arguments before the district court and that court's extensive analysis,[5] we deem it appropriate to rule on the merits of Novo's defense of invalidity. *See* 28 U.S.C. § 2106 (1994) ("The Supreme Court or any other court of appellate jurisdiction may . . . direct the entry of such appropriate judgment, decree, or order, or require such further

---

arg-arg-hGH, but none of the necessary experimentation is described in the specification, which is where it should be if it is to contribute to an enabling disclosure.

[5] Genentech stated that it would introduce new evidence at a full trial only in response to new arguments and new defenses raised by Novo. Novo revealed that it had no intention of raising any new arguments or defenses, stating that the "full and complete record" on appeal gave this court "the benefit of everything it really needs" to reach ultimate issues of validity. Thus, considerations that would normally dictate that we limit our decision to reversing the grant of the preliminary injunction are not present. *See University of Texas v. Camenisch*, 451 U.S. 390, 395 (1981) (stating that it is generally inappropriate to render a final judgment on the merits at the preliminary injunction stage because "a preliminary injunction is customarily granted on the basis of procedures that are less formal and *evidence that is less complete than in a trial on the merits.*") (citations omitted) (emphasis added).

proceedings to be had as may be just under the circumstances."); *Chicago Observer, Inc. v. City of Chicago*, 929 F.2d 325, 329 (7th Cir.1991) (reversing preliminary injunction and instructing district court to enter judgment in favor of defendant because the plaintiff "has not suggested that it holds more evidence it could offer at trial and we cannot imagine what additional evidence could aid its cause. Litigation is costly not only for the litigants but also for parties in other cases waiting in the queue for judicial attention. Once it becomes clear that additional proceedings are pointless, the court should bring the case to a close."). We therefore hold that claim 1 and hence the '199 patent are invalid as a matter of law for failure of the specification to enable the practice of the claimed method.

Novo has also argued that the '199 patent is invalid for lack of a written description of the claimed invention and that it is not infringed by Novo. Given our decision on the enablement question, we need not reach these issues.

B. *Other Factors*

Novo also challenges the district court's findings that irreparable harm, the equities, and the public interest favored Genentech. In view of our conclusion concerning the invalidity of the '199 patent, we need not consider these other findings.

CONCLUSION

The court abused its discretion by granting the preliminary injunction based upon an error of law. The district court's error was in finding that Genentech had shown a likelihood of success on the merits since the '199 patent is invalid for failure of the specification to meet the enablement requirement of § 112, ¶ 1. Accordingly, we vacate the injunction and instruct the district court to dismiss Genentech's claim for infringement of the '199 patent on the ground that the patent is invalid.

VACATED

APPENDIX B

Appendix B

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

GENENTECH, INC.,	:	Civil Action Nos.
Plaintiff,	:	95 Civ. 3474 (CBM)
v.	:	94 Civ. 8634 95 Civ. 0110
NOVO NORDISK A/S, NOVO NORDISK OF NORTH AMERICA, INC., NOVO NORDISK PHARMACEUTICALS INC., BIO-TECHNOLOGY GENERAL CORP., and BIO-TECHNOLOGY GENERAL (ISRAEL) LTD. ,	:	96 Civ. 1755 PRELIMINARY INJUNCTION ORDER
Defendants.	:	

ORDER OF PRELIMINARY INJUNCTION

This cause came on to be heard on Genentech's motion for a preliminary injunction in the above-titled consolidated actions and the court having considered the pleadings, the affidavits submitted in support of said motion and in opposition thereto, and having heard oral evidence and received exhibits in open court, and the court having made and filed its findings of fact and conclusions of law, it is

NOW ORDERED, ADJUDGED, and DECREED that

Novo Nordisk of North America, Inc., Novo Nordisk Pharmaceuticals, Inc., and Novo Nordisk A/S, and their parents, subsidiaries, agents, employees, attorneys and all those acting in concert with each of them who receive actual notice of this injunction order are hereby enjoined, pending the final determination of this action, from importing, making, using, selling, offering for sale or distributing in the United States,

Novo's Norditropin®, Human Growth Hormone product, except for current bona fide continuing Food & Drug Administration (FDA) approved clinical dosing trials.

This order shall be effective immediately upon payment by Genentech of cash or a surety bond that meets the satisfaction of the Clerk of the Court in the amount of [Text redacted by Court] pursuant to Federal Rule of Civil Procedure 65(c) or upon Genentech providing a letter by an officer with appropriate authority within thirty (30) days of the date of this order, guaranteeing payment by Genentech up to [Text redacted by Court]

SO ORDERED.

Dated: June 27, 1996
New York, New York

/s/ Constance Baker Motley

CONSTANCE BAKER MOTLEY
U.S.D.J.

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

GENENTECH, INC., Plaintiff, – against – NOVO NORDISK A/S, NOVO NORDISK OF NORTH AMERICA, INC., AND NOVO NORDISK PHARMACEUTICALS INC. Defendants.	Civil Action Nos. 95 Civ. 3474 (CBM) 94 Civ. 8634 95 Civ. 0110 96 Civ. 1755 OPINION

APPEARANCES:

Attorneys for Plaintiff Genentech, Inc.

ROGERS & WELLS
By: Leora Ben-Ami, Esq.
John E. Kidd, Esq.
Nicholas L. Coch, Esq.
Joseph Ferraro, Esq.
Philip E. Roux, Esq.
Gerard P. Norton, Esq.

Attorneys for Defendants Novo Nordisk A/S, Novo Nordisk of North America, Inc., and Novo Nordisk Pharmaceuticals, Inc.

GRAHAM & JAMES
By: Albert L. Jacobs, Jr., Esq.
Jesse D. Reingold, Esq.
Donald M. Currie, Esq.
Gerard F. Diebner, Esq.
Daniel A. Ladow, Esq.

MORGAN & FINNEGAN
By: John C. Vassil, Esq.
Kurt E. Richter, Esq.
Kenneth H. Sonnenfeld, Esq.

FINDINGS OF FACT AND CONCLUSIONS OF LAW

I. PRIOR PROCEEDINGS

1. This consolidated action began on November 30, 1994. On May 12, 1995, Genentech Inc. ("Genentech") moved for a temporary restraining order and a preliminary injunction to enjoin Novo Nordisk A/S, Novo Nordisk of North America, Inc., and Novo Nordisk Pharmaceuticals Inc.'s (collectively, "Novo"'s) importation, marketing and sale of Norditropin® in the United States based on Genentech's U.S. Patent No. 4,601,980 ("the '980 patent"). An evidentiary hearing was held before this court from May 22, 1995 until June 14, 1995.

2. On June 14, 1995, this court issued a temporary restraining order to preserve the *status quo* pending the Court's ruling on Genentech's motion for a preliminary injunction. On June 28, 1995, this motion was granted.[1]

3. Then, on February 26, 1996, the Federal Circuit issued its decision vacating the preliminary injunction and remanding the action to this court. *See Novo Nordisk of North America, Inc.* v. *Genentech, Inc.*, 77 F.3d 1364 (Fed. Cir. 1996). The Federal Circuit found that this court had applied an erroneous claim construction in determining that Genentech had established a likelihood of success on the merits of its patent infringement claim. Specifically, the Federal Circuit held that Claim 2 of the '980 patent, read in light of the specification, covers "only a method of directly expressing human growth hormone and does not encompass a cleavable fusion expression process." *Id.* at 1369.

4. The Federal Circuit did not analyze this court's findings and conclusions on the issues of validity, irreparable harm,

---

[1] The court assumes familiarity with this court's prior decision granting Genentech a preliminary injunction, *Novo Nordisk of North America, Inc.* v. *Genentech, Inc.*, Civil Action No. 94 Civ. 8634, 1995 U.S. Dist. LEXIS 12588 (S.D.N.Y. June 28, 1995), and the Federal Circuit's opinion vacating that decision. *Novo Nordisk of North America, Inc.* v. *Genentech, Inc.*, 77 F.3d 1364 (Fed. Cir. 1996).

balancing of equities, and public interest. Rather, the Federal Circuit set these conclusions aside because all were premised on an erroneous finding of infringement. *Id.* at 1371.

5. On March 21, 1996, Genentech again moved for a preliminary injunction prohibiting Novo from marketing and selling Norditropin® in the United States -- this time based on Novo's alleged infringement of U.S. Patent No. 5,424,199 ("the '199 patent"). A hearing on this motion was held from May 8, 1996 through May 23, 1996, and included concurrent testimony and evidence on Novo's motion to dismiss in *Genentech, Inc.* v. *Novo Nordisk A/S, et al.*, 96 Civ. 1755 (CBM), Genentech's separate action relating to the '199 patent. The court now addresses this motion.[2]

II. THE ISSUANCE AND HISTORY OF THE '199 Patent

6. The '199 patent was not before this court at the time of Genentech's original motion for a preliminary injunction because it did not issue until June 13, 1995 (GNE 200), the day

---

[2] Citations to "96 Tr. ___" are to the transcript of the hearing on Genentech's motion for a preliminary injunction based on the '199 patent held from May 8, 1996 through May 23, 1996. Citations to "95 Tr. ___" are to the transcript of the hearing on Genentech's previous motion for a preliminary injunction based on the '980 patent held from May 22, 1995 through June 14, 1995. The parties have stipulated that the evidence from the 1995 hearing can be utilized for purposes of Genentech's instant motion in its entirety (96 Tr. 56-57). "GNE ___" denotes Genentech Exhibits from the 1996 preliminary injunction hearing. "NN ___" denotes Novo Nordisk Exhibits from the 1996 preliminary injunction hearing. "Pl. Ex. ___" denotes Plaintiff ("Novo") Exhibits from the 1995 preliminary injunction hearing. "Def. Ex. ___" denotes Defendant ("Genentech") Exhibits from the 1995 preliminary injunction hearing. "FF ___" denotes the Court's findings of fact from its decision of *Novo Nordisk of North America, Inc.* v. *Genentech, Inc.*, Civil Action No. 94 Civ. 8634 (CBM), 1995 U.S. Dist. LEXIS 12588 (S.D.N.Y. June 28, 1995).

the evidentiary hearing concluded, and the day before the temporary restraining order was issued.[3]

7. The '199 patent arises out of the same pioneering invention as, and shares the specification of the '980 patent and the other patents which issued on the basis of the original Goeddel-Heyneker application filed July 5, 1979 (FF 58; 96 Tr. 515-516, Peet). The sole '199 patent claim, however, explicitly covers a cleavable fusion expression process. Novo has conceded this. (96 Tr. 1283, Villa-Komaroff). This claim reads as follows:

> 1. A method of producing a protein consisting essentially of amino acids 1-191 of human growth hormone comprising:
>
> (a) expressing in a transformant bacterium, DNA coding for a human growth hormone conjugate protein, which conjugate protein consists essentially of amino acids 1-191 of human growth hormone as set forth in combined FIGS. 1 and 3 unaccompanied by the leader sequence of human growth hormone or other extraneous protein bound thereto and an additional amino acid sequence which is specifically cleavable by enzymatic action, and
>
> (b) cleaving extracellularly said conjugate protein by enzymatic action to produce said protein consisting essentially of amino acids 1-191 of human growth hormone.

8. A patent applicant may apply for and obtain a series of patents based on the same application (96 Tr. 392, Peet). It is common practice for the applicant to obtain a series of different claims in separate patents covering different specific

---

[3] Genentech's '199 patent was not a device for extending the term of the '980 patent (96 Tr. 413, Peet). By reason of a terminal disclaimer filed by Genentech for the '199 patent, the '199 patent will expire on the same day as the earlier-issued '980 patent (96 Tr. 412-413, Peet).

embodiments until satisfied that the issued claims provide coverage for the full scope of the invention disclosed in the specification (96 Tr. 392, Peet). This is what Genentech did with the '199 patent (96 Tr. 392-93, Peet).

III. LIKELIHOOD OF SUCCESS ON THE MERITS

A. Claim Interpretation--The Scope Of Claim 1 Of The '199 Patent

9. The interpretation and construction of a patent claim, which define the scope of the patentee's rights under the patent, is a matter of law to be determined exclusively by the court. *Markman* v. *Westview Instruments, Inc.*, 52 F.3d 967, 970-971 (Fed. Cir. 1995) (en banc), *aff'd*, ____ U.S. ___, 116 S.Ct. 1384 (1996). To determine the meaning of claims, courts look to the claim language, the specification, and the prosecution history. *See, e.g., Minnesota Mining and Manufacturing Co.* v. *Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1576-77 (Fed. Cir. 1992). The prosecution history "is of primary significance in understanding the claims" because it provides an "'undisputed public record'" of the proceedings in the Patent and Trademark Office. *Markman*, 52 F.3d at 980. Additionally, claims should be interpreted as "those skilled in the art would interpret the claims." *Id.*

10. The parties agree that Claim 1 of the '199 patent covers a cleavable fusion expression process. However, Novo raised two issues regarding claim interpretation: (1) whether the term "DNA" and the reference to Figures 1 and 3 in the claim exclude the use of genomic DNA from the claim, and (2) whether the claim is a "means plus function" claim, therefore covering only the use of trypsin and the amino acid extensions recognized by trypsin and their "equivalents." For the reasons set forth below, the court finds that (1) the claim does not exclude genomic DNA and (2) enzymatic action is a generic term not limited to trypsin and its "equivalents" and the amino acid sequence is simply one which is specifically cleavable by the enzyme of choice.

1. Claim 1 Of The '199 Patent Contains No Limitation For The Source Of DNA Coding For Human Growth Hormone

11. The court rejects Novo's argument that Claim 1 of the '199 patent should be construed to contain a limitation on the source of the DNA utilized in the claimed process. No such limitation appears in the language of the claim (96 Tr. 396-397, Peet). Moreover, it is clear from the '199 patent prosecution history that both the Examiner and Genentech stated that the source of the DNA coding for human growth hormone was irrelevant and could include chemically synthesized DNA, cDNA or genomic DNA (GNE 201, pp. 83, 91). Indeed, this issue arose during prosecution of the '199 patent. The Examiner stated specifically his understanding that the DNA was generic and would include genomic DNA (GNE 201, p. 83). In response to a specific inquiry from the Examiner, Genentech stated that the source of the DNA was not critical and "need not be recited in the claims." (GNE 201, p. 91). Thus, the file history explicitly states that the claim of the '199 patent contained no limitation as to the source of the DNA, and can include genomic DNA (96 Tr. 396, Peet).

12. Novo also argues that the claim language "which conjugate protein consists essentially of amino acids 1-191 of human growth hormone as set forth in combined FIGS. 1 and 3" requires the use of semi-synthetic DNA, *i.e.*, a combination of synthetic DNA and cDNA, because the Figures show the preferred semi-synthetic DNA. Novo's argument, however, fails as a matter of simple grammatical construction. First, the phrase is set off by a comma from the DNA portion of the claim, indicating that the phrase modifies the conjugate protein, not the DNA. Second, Figures 1 and 3 show both a DNA sequence and an amino acid sequence. The claim language requires only that the hGH component of the conjugate *protein* be the amino acid sequence 1-191 disclosed in the referenced Figures. It does not require the particular example of the DNA for amino acids 1-191. Thus, the reference to the Figures has no bearing on the source of the DNA. The phrase relates only to the amino acid sequence.

13. Novo also argues that because the specification does not explicitly mention it, genomic DNA cannot be within the claim's scope (96 Tr. 1139, Villa-Komaroff). This argument is without merit. First, the claim language clearly does not require a particular source of DNA, as compared, for example, to the '832 patent, which does require a particular source, namely a combination of synthetic DNA and cDNA (NN 200). Second, although the specification refers to synthetic DNA and cDNA, Novo has conceded previously that everything in the specification is not necessarily in a claim (95 Tr. 1561, 1667-1668 Rzucidlo). The restriction requirement early in the prosecution of the parent '832 patent case distinguished as classes of inventions the use of semi-synthetic DNA to code for a protein (*i.e.*, the '832 patent) and the methods of making hGH (Pl. Ex. 56; 95 Tr. 1322-1324, 1667-1668, Rzucidlo)). Third, the prosecution history is clear that the claim is generic as to the source of DNA (GNE 201; pp. 83, 91; 96 Tr. 394-96, Peet).

14. Finally, the court has considered Novo's argument that because it was not known whether the genomic DNA coding for amino acids 1-23 was without introns and, therefore, useful,[4] the claim cannot include genomic DNA. The court finds this argument irrelevant. Methods to determine whether a genomic DNA sequence contained introns were known by 1979 (96 Tr. 1308-1311, Villa-Komaroff). Moreover, generic language in a claim can cover future improvements. *Bio-Technology General Corp.* v. *Genentech, Inc.*, 80 F.3d 1553, 1559 (Fed. Cir. 1996).

15. Therefore, the term "DNA coding for human growth hormone" in Claim 1 may include chemically synthesized DNA, cDNA, genomic DNA or any combination thereof. Furthermore, the claim's reference to "FIGS. 1 and 3" describes the amino acid sequence of the hGH component of the

---

[4] Introns are interrupting sequences in genomic DNA (96 Tr. 77-78, Falkinham).

conjugate protein and, therefore, does not limit the source of the DNA.

2. Claim 1 Of The '199 Patent Is Not A "Means Plus Function" Claim

16. Novo next argues that because the DNA coding for the conjugate protein is described in part by what it does (encodes the conjugate), the claim is a "means plus function" claim under 35 U.S.C. § 112(6). Novo then argues that because its process uses a different (and allegedly nonequivalent) amino extension and enzyme, it does not infringe. The court finds this claim characterization to be inconsistent with the claim, the specification and the prosecution history.

17. A "means plus function" claim is one in which a critical element is drafted so generally (as a "means for" or a "step for" performing a function) that the words alone cover all the means or methods for performing that function. *Jonsson* v. *Stanley Works*, 903 F.2d 812, 819 (Fed. Cir. 1990). However, not every claim including functional language is subject to § 112(6) analysis. *See*, *AMP, Inc.* v. *Fujitsu Microelectronics, Inc.*, 853 F. Supp. 808 (M.D. Pa. 1994) (the specific means language in the claim "'bus solder tail means' rather than just any means to accomplish the function" found not to trigger the application of § 112(6)). Even when one of the elements is recited in a claim using "means plus function" language, 35 U.S.C. § 112(6) applies only to that element, and not to the entire claim. *Johnston* v. *IVAC Corp.*, 885 F.2d 1574, 1580 (Fed. Cir. 1989). Claim 1 of the '199 patent is not a "means plus function" claim (96 Tr. 428-429, Peet). First, it does not contain the language that traditionally has been used in such claims. Second, the claim does not cover all means of encoding hGH but rather recites the required material--DNA. As the file history explains, the source of the material is not critical and is not limited, just as the source of the other starting materials are not limited (GNE 201, p. 91). Third, the claim covers only one of several possible processes for expressing human growth hormone--cleavable fusion.

18. The specification generally discloses the enzymes for performing extracellular cleavage. The '199 patent (col. 7, l.57-59) identifies trypsin by example (GNE 200). Similarly, the file history makes clear that both Genentech and the Examiner stated that Claim 1 covered enzymes generically (GNE 201, pp. 181, 194). In an office action dated July 9, 1993, the Examiner proposed to allow a claim limiting the enzyme to trypsin (*Id.* at 181). In response, Genentech stated that "trypsin must be regarded as a mere example of various enzymes that would be available in order to cleave the additional amino acids in the conjugate so as to give the 191 human growth hormone product after such cleavage" (*Id.* at 194). Genentech provided the Examiner with evidence showing not only the existence of many such enzymes, but also that those skilled in the art knew how to use them to effect specific cleavage (*Id.* at 156-162). Following Genentech's submission, the Examiner allowed the claim without the proposed limitation (*Id.* at 210-211). Thus, the claim cannot be reasonably construed as a "means plus function" claim as Novo suggests.

19. The cases relied upon by Novo to establish that Claim 1 of the '199 patent should be construed as a "means plus function" claim are distinguishable. In *Ex parte Maizel*, 27 U.S.P.Q.2d 1662 (Bd. Pat. App. 1993), the Board analogized the language "biologically functional equivalent thereof" to "means plus function" language. Unlike the instant case, neither the DNA nor the protein was defined. In the '199 patent, the end product, 1-191 hGH, is a specific amino acid sequence. *Fiers* v. *Revel*, 984 F.2d 1164 (Fed. Cir. 1993) did not involve 35 U.S.C. § 112(6); rather, the Court held that the patent claim at issue failed to meet the written description requirement of 35 U.S.C. § 112(1). Moreover, *Fiers* is clearly distinguishable because the patent claimed DNA whereas in the present case, the claim is to a method of making the protein. Likewise, *Genentech, Inc.* v. *Wellcome Found. Ltd*, 29 F.3d 1555 (Fed. Cir. 1994) is inapposite. *Genentech* also involved 35 U.S.C. § 112(1), not 35 U.S.C. § 112(6).

20. Moreover, even if Novo is correct, the designation of Claim 1 of the '199 patent as a "means plus function" claim would be of little help to Novo. 35 U.S.C. § 112(6) provides that a "means plus function" claim "shall be construed to cover the corresponding structure, material, or acts described in the specification *and equivalents thereof.*" As shown in more detail below, Novo's process for manufacturing hGH clearly uses equivalents to the enzymes and amino acid cleavage sites disclosed in the specification.

B. Novo's Infringement Of The '199 Patent

21. The determination of infringement is a two-step process. First, the language of the claims must be interpreted; second, the accused process must be compared to the interpreted claim language. *Read Corp.* v. *Portec, Inc.*, 970 F.2d 816, 821 (Fed. Cir. 1992) (citation omitted). In light of the language of Claim 1 of the '199 patent and Novo's Norditropin®'s process explained below, the court concludes that Genentech has shown a substantial likelihood of success on its infringement claim.

22. First, Novo's expert agreed that if the claim included genomic DNA and was not limited to particular enzymes, then Novo infringes (96 Tr. 1270-71, Villa-Komaroff). Thus, the issues to be decided at this juncture are narrow. Since Genentech has made a substantial showing that "DNA" may include genomic DNA and the enzyme for cleavage is not limited, it follows that Genetech has made a substantial showing of infringement.

23. In making the accused product Norditropin®, Novo utilizes cDNA encoding amino acids 24-191 of hGH (96 Tr. 96-97, 106-107, Falkinham; 95 Tr. 581, Dalboge). Novo utilizes a genomic DNA fragment encoding amino acids 1-23 of human growth hormone which does not contain introns (96 Tr. 98-100, Falkinham; 95 Tr. 621-622, Dalboge). The genomic DNA is interchangeable with synthetic DNA (96 Tr. 172-174, Falkinham; 96 Tr. 395-397, Peet; 96 Tr. 1312, Villa-Komaroff). In addition, Novo chemically synthesizes nucleotides coding for an additional amino acid sequence [Text

redacted by Court] which is specifically cleavable by enzymatic action (96 Tr. 95-104, Falkinham). The three pieces--cDNA, genomic DNA, and chemically synthesized DNA--code for a conjugate protein (96 Tr. 133-137, Falkinham; 95 Tr. 1353-1356, 1360 Rzucidlo; GNE 210). This DNA is introduced into a plasmid (Def. Ex. 72, 126, 95 Tr. 128-146, Falkinham; 95 Tr. 617-623, Dalboge).

24. Novo next places the recombinant plasmid in a bacterial host, E. coli, to express DNA coding for the conjugate protein [Text redacted by Court] hGH (95 Tr. 135-36, Falkinham).

25. Following the expression of DNA coding for conjugate protein [Text redacted by Court] -hGH, the bacterial host has within it the conjugate protein [Text redacted by Court] -hGH (95 Tr. 137- 138, 96 Tr. 104, Falkinham). Novo then conducts an isolation and purification process, during which Novo utilizes enzymatic action to cleave, outside of the cell, the [Text redacted by Court] extension, using an enzyme called [Text redacted by Court] (95 Tr. 139-140, 96 Tr. 137, 139-145, Falkinham; GNE 211). After cleaving the[Text redacted by Court], Novo is left with amino acids 1-191 of human growth hormone (*Id.*).

26. Based on its proposed claim construction, Novo argues that its process for manufacturing Norditropin® does not infringe Claim 1 of the '199 patent because it uses genomic DNA, rather than synthetic DNA, for a certain portion of its DNA sequence, and because it uses a different cleavage site and [Text redacted by Court], rather than trypsin, for cleavage. However, as shown above, Claim 1 of the '199 patent contains no limitations with respect to either the source of the DNA or the enzymes utilized in the cleavage process and Novo's [Text redacted by Court] is specifically cleavable. Therefore, Novo's argument fails.

27. Moreover, even if Novo is correct in characterizing Claim 1 of the '199 patent as a "means plus function" claim, Genentech has made a substantial showing that Novo nonetheless literally infringes each and every element of the claim.

Novo in its brief states that the alleged "means plus function" nature of the claim only limits the type of enzyme and amino extension which can be used. Novo did not argue that section 112(6) limited the source of the DNA--thus, this issue is not before the court. In any event, the genomic and synthetic DNA encoding amino acids 1-23 of hGH are interchangeable (*see*, *supra*). The enzyme [Text redacted by Court] is equivalent to trypsin for purposes of the process of Claim 1 of the '199 patent (GNE 201, p. 158; 96 Tr. 167-170, Falkinham; 96 Tr. 347-349, Ravetch). The [Text redacted by Court] extension of Novo's conjugate is similarly equivalent to the disclosed arg-arg or lys-lys cleavage sites taught in the '199 patent. In both cases, the sequences were chosen because the enzyme would specifically cleave them and, in fact, both sequences contain [Text redacted by Court], a choice [Text redacted by Court] (*see*, *infra* at p. 23). Therefore, even if Claim 1 is construed as a "means plus function" claim, Novo does not avoid a finding of literal infringement. *See Texas Instruments, Inc.* v. *United States Trade Commission*, 805 F.2d 1558, 1571 (Fed. Cir. 1986).

28. Novo contends that its process involves various purported improvements over the process of the '199 patent, such as how to tailor genomic DNA and the specific amino extension and cleavage enzyme (96 Tr. 1127, 1149, 1201, Villa-Komaroff). Assuming that the Novo process may employ improvements, Genentech still enjoys a likelihood of success on the merits of its claim that Novo's improved process nonetheless infringes. It is hornbook law that the development of patentable improvements to a process does not avoid infringing a dominant patent. *See Bio-Technology*, 80 F.3d at 1559-60; *Atlas Powder Co.* v. *E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1580 (Fed. Cir. 1984). Furthermore, as the Federal Circuit has held, "'an embellishment' made possible by technological advances may not permit an accused device to escape 'the web of infringement.'" *Datascope Corp.* v. *SMEC, Inc.*, 776 F.2d 320, 326 (Fed. Cir. 1985), cert. denied, 493 U.S. 1024 (1990).

29. Based on the foregoing, Genentech has satisfied the requirements necessary to entitle it to a preliminary injunction. Genentech's evidence strongly supports its claim that Novo's process for making hGH literally infringes Claim 1 of the '199 patent. Novo's cultured bacterial transformants will express DNA coding for a hGH conjugate protein as specified in Claim 1 because its DNA sequence codes for amino acids 1-191 of hGH and an additional amino acid sequence which is specifically cleavable by enzymatic action (95 Tr. 608-609, Dalboge). Following expression, Novo cleaves, outside of the cell, the hGH conjugate protein to produce amino acids 1-191 of hGH (95 Tr. 141-143, 96 Tr. 137, Falkinham; 95 Tr. 610, Dalboge; GNE 210).

C. Genentech Did Not Disclaim Cleavable Fusion Expression

30. Finally, Novo raises the issue of "prosecution history estoppel"-- *i.e.*, whether by limiting Claim 2 of the '980 patent claim to direct expression, Genentech forever surrendered its right to claim cleavable fusion expression in the '199 patent. Novo's argument is specious. It is routine practice to accept certain claims which the Patent Office indicates are allowable and to continue the examination process with continuation applications to seek further claims (96 Tr. 412-413, Peet). No argument or amendment was made which forever precluded Genentech from seeking coverage of the cleavable fusion expression embodiment taught in the patent (96 Tr. 392-393, Peet).

31. The Federal Circuit decision, which held that the language used in Genentech's '980 patent claimed only direct expression, does not prevent Genentech from prevailing on the instant claim. Novo, 77 F.3d at 1369-70. In fact, the Court's statement that the patent teaches cleavable fusion expression, but did not claim it, suggests that a further application to this alternative embodiment is proper. *Id.* at 1369.

32. Finally, Novo's cited cases do not suggest another result. This is not a case where applicant narrowed his claim during prosecution and then sought broader coverage under

the doctrine of equivalents. *See, Mark I Marketing Corp.* v. *R.R. Donnelley & Sons Co.*, 66 F.3d 285, 291 (Fed. Cir. 1995), *cert. denied*, ___ U.S. ___, 116 S. Ct. 917 (1996). Nor is this a case where applicants declared that certain subject matter did not work in order to achieve allowance of claims and later sought to cover the supposedly unworkable subject matter. *Texas Instruments Inc.* v. *United States International Trade Commission*, 988 F.2d 1165, 1173-75 (Fed. Cir. 1993). Genentech only argued that *uncleavable* hGH conjugates did not work (95 Tr. 1907-1908, Falkinham; 96 Tr. 406-407; 415-416, Peet). Nor is this a case where the inventor defined a term as limited to a single embodiment and was later held to that definition. *Abtox, Inc.* v. *Exitron Corp.*, 899 F. Supp. 775, 780 (D. Mass. 1995).

33. Thus, the prosecution history of the '980 patent, as interpreted by the Federal Circuit, did not preclude Genentech from seeking claims to cleavable fusion expression in the '199 patent. As explained above, the court finds that there is a strong likelihood that Genentech will prevail on the merits of its infringement claim.

D. Validity Of The '199 Patent

34. The '199 patent is presumed valid under 35 U.S.C. § 282. Genentech's likelihood of success must be determined in the context of Novo's ultimate burden to establish invalidity by clear and convincing proof. *Orthokinetics, Inc.* v. *Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1570 (Fed. Cir. 1986). That is, to be entitled to injunctive relief, Genentech must show that it is likely that Novo will not prove invalidity by clear and convincing evidence. Genentech has met this burden.

35. The burden is on Novo to come forward with an affirmative defense to the validity of the patent. *Roper Corp.*, v. *Litton Systems, Inc.*, 757 F.2d 1266, 1270 (Fed. Cir. 1985); *New England Braiding Co., Inc.* v. *A.W. Chesterton Co.*, 970 F.2d 878, 882 (Fed. Cir. 1992). Novo did not challenge the validity of the '199 patent under 35 U.S.C. § 102 and/or 103. Novo's sole challenge to validity is based on 35 U.S.C. §

112(1)--purported lack of enablement and lack of written description or support.

36. In *Novo*, the Federal Circuit held that the '980 patent specification contains support for the production of hGH by "cleavable fusion" expression:

> The specification teaches, for example, that the invention allows the "expression of either the intended product absent extraneous conjugated protein [i.e., by direct expression], or intended product conjugated to but specifically cleavable from extraneous protein [i.e., by cleavable fusion expression]." Col. 7, 11, 48-51.

77 F.3d at 1369. The Federal Circuit never determined that the specification of the '980 patent did not contain sufficient teachings to enable one skilled in the art to utilize a cleavable fusion expression process to make hGH. Rather, the Federal Circuit acknowledged the teachings of the patent specification, and found it unnecessary to determine whether these teachings were sufficient to satisfy the requirements of 35 U.S.C. § 112.

37. Moreover, the Federal Circuit noted that a patentee may claim something narrower than the full scope of the invention taught by the specification:

> While claims are to be interpreted in light of the specification, all that appears in the specification is not necessarily within the scope of the claims and thus entitled to protection. What is not claimed, even though disclosed as part of the "invention," cannot be enjoined. *Id.* at 1369.

38. Novo's 35 U.S.C. § 112(1) challenge raises several related arguments on invalidity. First, Novo contends that *Novo* is the "law of the case" and establishes lack of "support." Second, Novo argues that the '199 patent does not contain enough information for one skilled in the art to practice cleavable fusion hGH expression without "undue experimentation." Finally, Novo contends that the '199 patent lacks an

adequate written description to show that the inventors were in possession of the invention of cleavable fusion hGH expression at the time of filing; thus, Novo argues that the '199 patent represents an "incomplete conception." These arguments are legally and factually incorrect.

1. Novo's Law Of The Case Argument Is Without Merit

39. The "law of the case" doctrine applies to legal questions determined on appeal in the same case. *Arizona* v. *California*, 460 U.S. 605 (1983). Here, the only legal question decided by the Federal Circuit in the prior appeal concerned the interpretation of Claim 2 of the '980 patent. Whether a patent specification contains "support" for claim language (i.e., whether the specification provides a sufficient written description or enablement) includes questions of fact. *In re Alton*, 76 F.3d 1168, 1171-72 (Fed. Cir. 1996) ("[t]he issue of whether a patent specification adequately describes the subject matter claimed is a question of fact") (citation omitted); *Novo*, 77 F.3d at 1371 (the Federal Circuit stated that determining whether a patent specification was enabling would require "resolution of factual questions").

40. Moreover, the "law of the case" is not to be applied in draconian fashion from an appeal in a preliminary injunction setting.[5] Generally, rulings on tentative and extraordinary relief (such as preliminary injunctions) do not trigger "law of the case" consequences. This is because such rulings represent, by definition, a preliminary rather than final adjudication

---

[5] The cases cited by Novo in its opposition papers, *In re Ivan F. Boesky Securities Litigation*, 957 F.2d 65 (2d Cir. 1992) and *Smith International, Inc.* v. *Hughes Tool Co.*, 759 F.2d 1572 (Fed. Cir.), *cert. denied*, 474 U.S. 827 (1985) are inapposite. Neither dealt with the application of law of the case in a preliminary injunction setting. Indeed, both state that the presentation of different evidence is a basis for *not* applying law of the case in a subsequent trial or proceeding. A substantial amount of different evidence was presented in this preliminary injunction hearing on the issues of enablement and written description.

on the merits. *See University of Texas* v. *Camenisch*, 451 U.S. 390, 395 (1981); *Goodheart Clothing Co., Inc.* v. *Laura Goodman Enters., Inc.*, 962 F.2d 268, 274 (2d Cir.1992); *Consumers Union of United States, Inc.* v. *New Regina Corp.*, 664 F. Supp. 753, 760 (S.D.N.Y. 1987).

41. Novo's argument is premised on the statement by the Federal Circuit that the "broad reading of Claim 2" of the '980 patent was not supported by the specification and prosecution history. Novo overreaches when it attempts to transform the Court's statement into one conclusively determining whether there is support for a new and different claim in another patent. The Court did not conclusively address the written description or enablement for enzymatic cleavable fusion expression. *Novo*, 77 F.3d at 1364. A close and fair reading of the Federal Circuit's decision shows that the Court relied upon the specification only for the determination that the phrase "unaccompanied by . . . bound thereto" was defined by the specification as direct expression. *Id.* at 1369. The Court, on the issue of whether the specification otherwise described cleavable fusion expression, stated that the '980 (and thus the '199) patent specification "taught" cleavable fusion expression. *Id.* Thus, applying the "law of the case" doctrine to the Federal Circuit's decision in *Novo* would not only be inappropriate, it would misrepresent the content of that decision.

2. Novo's Contention That The '199 Patent Is Invalid For Lack Of Enablement Is Without Merit

42. Novo also contends that the '199 patent is invalid for lack of enablement, based on a supposed lack of specificity and detail regarding cleavable fusion expression in the '199 patent. This contention is erroneous.

43. Novo pays little heed to the Federal Circuit statement in the prior appeal that the '980 patent taught cleavable fusion expression. The "lack of enablement" issue was raised, and resolved in Genentech's favor, by the Patent Office during examination of the '199 patent application (GNE 201, pp. 137-138, 155-162, 175-177, 187-198, 210-211, 234).

Additionally, this court has already made findings on enablement in the earlier preliminary injunction, having heard Novo's expert testimony on the issue, which contradict Novo's present position (FF 97-98). This court has considered the enablement issue again based on the above as well as the new evidence of record, keeping in mind that Genentech's burden on this issue is to establish a likelihood that Novo will not ultimately prove this defense by clear and convincing evidence.

a. The '199 Patent Enables One To Practice The Claim Without Undue Experimentation

44. A patent is enabled if the patent disclosure would allow one of ordinary skill in the art to practice the claimed invention without undue experimentation. *See* 35 U.S.C. sec. 112; *Scripps Clinic & Research Found.* v. *Genentech, Inc.*, 927 F.2d 1565, 1571 (Fed. Cir. 1991). In considering enablement, the person of ordinary skill is assumed to know what is available in the art. *Id.* at 1571. The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art, without undue experimentation. *United States* v. *Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989) (citations omitted). Some experimentation is allowable because patent specifications are not supposed to be production specifications. *See, e.g., Northern Telecom, Inc.* v. *Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir.), *cert. denied*, 498 U.S. 920 (1990). Additionally, a patent specification need not teach, and preferably omits, what is well-known in the art. *Hybritech Inc.* v. *Monoclonal Antibodies Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987).

45. Enablement is not precluded by the necessity for some experimentation such as routine screening. *Du Pont*, 750 F.2d at 1576. However, the experimentation needed for practicing the invention must not be "undue." *Hybritech*, 802 F.2d at 1384; *In re Angstadt*, 537 F.2d 498, 502-504 (C.C.P.A.1976). Determining what constitutes undue experimentation in a

given case requires the application of a standard of reasonableness, giving due regard for the nature of the invention and the state of the art. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (citations omitted). The test is not merely quantitative, since a considerable amount of experimentation is permissible if it is routine. *Ex parte Jackson, et al.*, 217 U.S.P.Q., 804, 807 (Bd. App. 1982). Whether undue experimentation is needed is not a single factual determination, but rather a conclusion reached by weighing many factual considerations, including (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims. *In re Wands*, 858 F.2d at 737.

46. Accordingly, it is evident that one skilled in the art in 1979, using the '199 patent and knowledge in the art, would have been able to practice the claimed invention without undue experimentation. This is primarily because (1) any experimentation needed would have been merely routine and within the norm expected in the field; (2) the art of using enzymes to cleave proteins was well established and predictable; (3) the patent provided guidance both for the creation and expression of the desired DNA and for one skilled in the art to use known enzymes and purification techniques to cleave an amino extended hGH; and (4) the relative skill of those in the art was quite high.

47. The court is mindful of the fact that the foundation of the '199 patent was that it was the first creation of a recombinant gene encoding 1-191 hGH without a bioinactivating leader (95 Tr. 1138, Villa-Komaroff). The nature of the invention claimed in the '199 patent is a combination of that breakthrough -- the useful DNA sequence encoding 1-191 hGH -- with other known elements (GNE 201, p. 203). Novo does not argue that the breakthrough achievement -- obtaining DNA encoding 1-191 hGH -- is not enabled. Rather it is the portion of the claim relating to the well-known, conventional technology of enzymatic cleavage of the resulting protein that

Novo argues is not enabled by the '199 patent. Novo's arguments are directed to an aspect of the claimed invention which is relatively focused -- *i.e.*, the extracellular, enzymatic cleavage of an additional amino acid sequence from a specific amino acid sequence (hGH). This court rejects Novo's position.

i. The Level of Skill In The Art

48. Both parties agree that one of ordinary skill in the art as of the July 5th, 1979 filing date of the '199 patent was someone who would have completed a doctoral degree and have begun post-doctoral training in the area of molecular biochemistry or genetics (96 Tr. 280-281, Ravetch; 96 Tr. 1131, Villa- Komaroff).

ii. The '199 Patent Provides Both Guidance And Direction For Producing Cleavable Fusion Expression Of hGH

49. To obtain a cleavable fusion protein expression product, DNA for the intended protein is linked to DNA which codes for an additional amino acid sequence (96 Tr. 116-17, 125, Falkinham; 1180, Villa-Komaroff).

50. The '199 patent describes the manipulation of DNA fragments, by cleavage and ligation, to obtain a desired DNA sequence (GNE 200, col. 1, line 55-col. 2, line 22; Figure 5; 96 Tr. 281-285 Ravetch). The joining of DNA fragments by either blunt end or cohesive end ligation was well known in the art by July 1979 (96 Tr. 285, Ravetch). The patent contains a specific example of the DNA for 1-191 hGH as well as the methodology used to make the DNA (GNE 200, col. 8, line 32-col. 12, line 15).

51. The evidence adduced at the hearing supports the conclusion that the '199 patent, the prior art and the knowledge in the art all provide sufficient enablement for one skilled in the art to synthesize and link DNA encoding an additional amino acid sequence to the DNA encoding hGH (95 Tr. 1141-1143, Villa-Komaroff). Designing such DNA sequences is taught in the patent and the art (GNE 200, col. 6), and one skilled in the

art would have been able to design such sequences using the disclosed DNA (and resulting amino acid sequences) set forth in Figures 1 and 3 of the '199 patent, as well as the well-known genetic code (96 Tr. 293-296, Ravetch). The '199 patent also describes where the DNA coding for the desired cleavage site should be placed in relation to the DNA for the desired protein product (96 Tr. 295-296, Ravetch; GNE 201, col. 7, lines 52-59). Dr. Ravetch explained how one skilled in the art in 1979 would have proceeded to make a DNA sequence coding for 1-191 hGH with an additional trypsin-cleavable met-arg-arg cleavage site using the teachings of the '199 patent (96 Tr. 286-293; 295-297, Ravetch; GNE 232).

52. In view of the prior art, the '199 patent is sufficient to allow one of reasonable skill to make a cleavable conjugate and to create a cleavable fusion protein by 1979.

iii. The Use Of Trypsin To Obtain 1-191 hGH Involved Only Routine Application Of Predictable Art

53. Trypsin is the only enzyme for protein cleavage specifically referred to in the '199 patent (GNE 200, col. 7, line 58). As of 1979, trypsin was a well-known and widely studied, characterized and used enzyme, whose existence had been known for over fifty years (96 Tr. 298, 317-326, Ravetch; GNE 223, GNE 229, GNE 228, GNE 225, GNE 226 and GNE 230). The conditions for the use of trypsin, including temperature, pH, etc., were recited in package inserts which accompanied each purchase of trypsin, as well as in the "standard cookbooks" which described trypsin and many other enzymes and their conditions for use (96 Tr. 325-330, Ravetch; GNE 219, GNE 229, GNE 244). The evidence showed that trypsin was in widespread application and use in laboratories around the world in 1979.

54. Genentech's expert testified in detail as to how one skilled in the art would have been able to practice cleavable fusion expression to obtain a trypsin-cleavable conjugate fusion protein which, when cleaved by trypsin, would yield

1-191 hGH (96 Tr. 299-305, Ravetch; GNE 219, GNE 220). Although there are twenty potential trypsin cleavage sites in 1-191 hGH (96 Tr. 367, Ravetch; 96 Tr. 1194, Villa-Komaroff), as of 1979, there were well-known, routine methods for controlling the action of enzymes, including trypsin, in order to alter the specificity of cleavage at different sites in the protein (96 Tr. 301, Ravetch; GNE 219). One method of controlling the cleavage at sites in the protein is by "partial proteolysis" or partial digestion (96 Tr. 302-304, Ravetch). Partial proteolysis was an extremely well-known technique in 1979, used routinely by molecular biologists and taught in general college biology texts (*Id.*). It is disclosed in the '199 specification by reference to a Great Britain application (GNE 200, col. 7, lines 57-59). Using partial proteolysis, it was known to modify the enzymatic reaction conditions so that cleavage of the protein occurs on the average of just once per molecule, i.e., once per protein chain (96 Tr. 303, Ravetch). As a result of such use of partial proteolysis, and using trypsin as a cleavage agent to cleave an amino acid extension of arg-arg from the 1-191 amino acids of hGH, a population of proteins will be obtained which includes at least some 1-191 amino acid hGH (96 Tr. 303-304, Ravetch). Novo's expert agreed with this analysis (96 Tr. 1230-31, Villa-Komaroff, NN 269). Novo's expert, for example, testified that 5% of the product would be 1-191 hGH. *Id.*

55. Thus, by using the teachings of the '199 patent and the specific example of trypsin and an arg-arg amino acid extension, and the well-known method of partial proteolysis, one skilled in the art would have been able to produce 1-191 hGH.

56. Novo argues, however, that although Claim 1 of the '199 patent does not recite any "recovery" step for the 1-191 hGH, Claim 1 is not enabled because it necessarily requires "recovery" of 1-191 hGH from the mix in order to be useful. Novo's argument is that although the claim does not require pure hGH or hGH with clinical utility, the enablement requirement -- that the patent enable the invention to be used -- requires purification to the point of clinical utility for humans. This argument must be rejected since the Federal Circuit has

said that such clinical utility is not required. *In re Brana*, 51 F.3d 1560, 1568 (Fed. Cir. 1995) ("Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans"). Novo has never explained why the hGH made had no utility at all.

57. In any case, recovery of 1-191 hGH was enabled. From the population of protein fragments, one skilled in the art in 1979 would have been able to retrieve the 1-191 hGH from all of the other members of the protein population (96 Tr. 305-306, Ravetch). The methods for separation of proteins were well-known in 1979, and the separation could be effected using, *inter alia*, the different sizes to separate the proteins and/or the different charges (some proteins are more negative, and some are more positive) (96 Tr. 305-306, Ravetch). The '199 patent, from col. 13, line 18 to col. 14, line 4, describes methods which either singly or in combination would be used to obtain 1-191 human growth hormone from a population of amino acid products (96 Tr. 306-307, Ravetch). Molecular biologists in this field at the time of the '199 invention were highly trained and were familiar with finding and purifying proteins using these techniques (GNE 225; 96 Tr. 1202, 1288-89, 1332-1334, 1343-1346, Villa-Komaroff). Both parties agreed that purification techniques such as column chromatography were known and used by such scientists (96 Tr. 1290, Villa- Komaroff).

58. Indeed, in the Novo process, Novo obtains a mixture of [Text redacted by Court] and hGH, which can be easily separated by [Text redacted by Court] (96 Tr. 1336, Villa-Komaroff, 95 Tr. 572-73, Dalboge) a method cited by the '199 patent, because the amino extension [Text redacted by Court] The examples in the '199 patent, arg-arg and lys-lys also contain [Text redacted by Court] (96 Tr. 1343-1345, Villa-Komaroff).

59. The court therefore finds that, even if Novo's "recovery" requirement was accepted, based upon what was taught in the '199 patent, and using those teachings in conjunction with the partial proteolysis technique which was well-known in the art at the time, one skilled in the art would have been able to create a cleavable fusion hGH protein as denoted in the patent which would be cleaved with trypsin and yield 1-191 amino acid hGH and that the 1-191 hGH could be recovered without undue experimentation.

60. There is no clear difference of opinion on this issue. While Novo's expert originally stated that it would be impossible to separate out the hGH, on cross examination she readily agreed that the sample could be at least partially purified (96 Tr. 1332-1334, Villa-Komaroff). Thereafter, she questioned whether the ultimate purification would lead to pure hGH (96 Tr. 1343-1346, Villa-Komaroff). In the end, however, the most that she could say was that it was possible but she was "not sure" (96 Tr. 1347, Villa-Komaroff). This was one of several occasions where Novo's expert's testimony on scientific matters was inconsistent (*See* 96 Tr. 1166-68, 1266-67, 1284-88 Villa- Komaroff). Dr. Ravetch's testimony that such purification would have been routine and predictable, in contrast, was compelling and not called into question on cross-examination. Thus, based on the scientific testimony, as well as the experts' demeanor and credibility, the court finds that the claim is enabled.

61. Additionally, in 1979 there were other known methods to increase the specificity of trypsin (and other proteins) so that one could obtain the 1-191 hGH in higher yield (96 Tr. 307-311, Ravetch; GNE 200 at col. 7, 57-59, citing GB 2008123A; GNE 222). For example, one could block either the lysine sites or the arginine sites, so that under the well-known partial proteolysis conditions, the population of protein chains which was obtained was altered, thereby increasing the yield of the desired hGH (96 Tr. 308-310, Ravetch). Unblocking the amino acids was similarly well-known in 1979 (96 Tr. 316-317, Ravetch; GNE 220, GNE 229, p. 63). The 1-191 hGH would be recovered

according to well-known techniques known in the art and described in the '199 patent.

62. The court finds that the use of trypsin to obtain 1-191 hGH involved only the routine application of predictable enzyme art to the invention described in the '199 patent.

iv. The Use Of Enzymes Other Than Trypsin To Produce 1-191 hGH Is Enabled

63. The '199 patent refers to trypsin by way of example (GNE 200, col. 7, line 58). Trypsin was the prototype enzyme for the class of enzymes that cleave protein molecules through the mechanism of peptide bond hydrolysis and is representative of that class of enzymes (96 Tr. 331-332, Ravetch). In the literature, trypsin is referenced as exemplary of the class of proteolytic enzymes (96 Tr. 332-335, Ravetch; GNE 225, 228). Proteolytic enzymes are enzymes which are able to cut protein molecules at their peptide bonds (96 Tr. 338, Ravetch). All proteolytic enzymes are quite similar in their action, and within the general group of proteolytic enzymes there are both exopeptidases and endopeptidases (96 Tr. 338-339, Ravetch). In the literature prior to July 1979, including literature referenced in the '199 patent, the similarity of exopeptidases and endopeptidases is described (96 Tr. 340-343, 345-346, Ravetch; GNE 227).

64. Also in the literature known to those skilled in the art as of July 1979, many proteolytic enzymes are referenced, including trypsin, chymotrypsin, dipeptidase, aminopeptidase, carboxypeptidase, thermolysin, elastase, pepsin, leucine aminopeptidase, papain, subtilisin (96 Tr. 335-336, Ravetch). Indeed, all of these specific enzymes (and more) are referenced in Sidney P. Colowick and Nathan O. Kaplan, *Methods of Enzymology* (GNE 221 and 229) which contain extensive detail of the characteristics and use of the proteolytic enzymes, including the specific amino acid sequence the enzymes recognize and the favored reaction conditions for the enzymes, such as pH and temperature (96 Tr. 336-337, Ravetch). Novo's expert admitted on cross-examination that if one chose not to use trypsin, it would have been reasonable to

use books like *Methods of Enzymology* and pick another enzyme (96 Tr. 1342-43 Villa-Komaroff, GNE 320). The reasonableness of this approach is probative of its predictability.

65. The court finds that for purposes of cleavage by enzymatic action recited in the '199 patent, the activities of exopeptidases and endopeptidases are the same.

66. In the '199 patent a Great Britain patent application no. 2008123A is referenced for further information on cleavage (GNE 200, col. 7, line 58). This GB 2008123A provides examples of both endopeptidases and exopeptidases (96 Tr. 345-346, Ravetch), as well as of the techniques of partial hydrolysis (96 Tr. 346-347, Ravetch) and blocking (or protecting) lysine sites to increase the yield of the desired protein (96 Tr. 347-348, Ravetch).

67. The specific enzyme used by Novo, [Text redacted by Court] is referenced throughout the literature prior to 1979 (96 Tr. 348-352, Ravetch). In the file history of the '199 patent, Genentech provided extensive lists of peptidases known in 1979 to the Examiner. Genentech stated that trypsin was an example and that "[m]any additional and equivalent peptidases are listed, both those capable of hydrolysing single residues and those capable of cleaving dipeptide or multipeptide units either from the N-terminus or the C-terminus. . . ." (GNE 201 p. 158). Thus, in the file history, Genentech stated that for its purposes [Text redacted by Court] was considered an additional and equivalent enzyme to trypsin (96 Tr. 1316, Villa-Komaroff). The court finds that the specific enzyme used by Novo to perform extracellular cleavage falls squarely within the categories of enzymes included within in the '199 patent and known in the art in 1979.

68. The use of enterokinase to cleave amino extended hGH, referencing 1977 and 1979 publications, was performed by Eli Lilly (GNE 320). It was also known since 1974 that the enzyme plasmin would cut hGH only twice making purification easier than with trypsin (GNE 321). These instances are probative on the issue of the predictability and reasonableness

of using enzymes other than trypsin to produce 1-191 hGH from a cleavable fusion protein product.

69. In sum, the court finds that in 1979 one skilled in the art would have been able, using the '199 patent and the knowledge in the art, to construct DNA that would encode a cleavable fusion protein of specifically cleavable amino acids in conjunction with 1-191 hGH. When the conjugate was expressed and then cleaved extracellularly, the process would result in the liberation of the 1-191 hGH. This process is enabled for any number of enzymes in addition to trypsin.

v. The Absence Of An Actual Experiment Of Cleavable Fusion Expression Does Not Establish Lack of Enablement

70. Novo argues that Claim 1 of the '199 patent is not enabled because it does not contain a "working example" of cleavable fusion expression (NN 201). Novo contends that in the '199 patent, cleavable fusion examples are "merely prophetic" and they do not aid one skilled in the art in practicing the invention. Because they are prophetic, argues Novo, there can be no guarantee that the examples would actually work. However, the Federal Circuit has held that the "[u]se of prophetic examples, however, does not automatically make a patent nonenabling." *Du Pont*, 750 F.2d at 1577. "The burden is on one challenging validity to show by clear and convincing evidence that the prophetic examples together with other parts of the specification are not enabling." *Id.*

71. The '199 patent describes in detail the methods and techniques for obtaining DNA encoding for 1-191 hGH, as well as the methods and techniques for attaching additional DNA sequences (coding for additional amino acid sequences) to that DNA. The '199 patent also identifies trypsin as a representative example of a cleavage agent, as well as the amino acids which trypsin cleaves. Therefore, the court finds that the '199 patent describes an example of creating a DNA sequence which would encode for, *inter alia*, met-arg-arg-1-191 hGH which in turn, by standard techniques, could be cleaved using trypsin to obtain 1-191 hGH. Merely because this example,

which works, was not actually performed prior to the July 5, 1979 filing date of the '199 patent does not detract from this disclosure.

72. Moreover, Novo's expert agreed that in 1979 one skilled in the art desiring an amino acid sequence which would be specifically cleavable by enzymatic action would look to the literature such as Sidney P. Colowick and Nathan O. Kaplan, *Methods of Enzymology* and pick out a sequence and enzyme that would have the best chance of working (96 Tr. 1327, Villa-Komaroff). The statement in the specification "for example trypsin" tells one of ordinary skill in the art to do so (GNE 200, col. 7, lines 57-59). Novo's expert's basic disagreement with Genentech is simply that until the experiment was done, it was not certain that the experiment would work (96 Tr. 1327, 1329, Villa-Komaroff). This is irrelevant to enablement, however, where the inquiry is whether undue experimentation is required.

73. Novo's expert stated that the trypsin example was nonenabling by defining specifically cleavable as having only one cleavage site (96 Tr. 1173, Villa-Komaroff). Using this definition Novo's expert admitted that even the specific example given in the patent (using trypsin to cleave at arginines) would not fit the claim and the claim would cover nothing at all (96 Tr. 1283, Villa-Komaroff). Novo's same expert testified similarly at the 1995 hearing that the '980 patent covered nothing (95 Tr. 1142, Villa-Komaroff). The court rejects this testimony as not credible and against the weight of the technical knowledge in the art. The record is replete with evidence that "specifically cleavable" means that a specific amino acid sequence is recognizable for enzyme attack, not that there is only one site for cleavage (*See, e.g.*, GNE 200; GNE 229).

vi. Novo's Remaining Non-Enablement Arguments Lack Merit

74. Novo argues that the '199 patent is not enabling because it did not teach one how to construct Novo's specific synthetic amino-extension or how to cleave that amino extension from the amino acids encoding hGH using [Text redacted

by Court] (95 Tr. 1141, Villa-Komaroff; 96 Tr. 1127-1129, 1180, Villa-Komaroff). However, Novo's own expert admitted that by the time of the '199 invention, those skilled in the art knew how to synthesize an amino extension with a start codon, such as Novo's [Text redacted by Court] (95 Tr. 1141-1143, Villa-Komaroff). Moreover, the testimony of Genentech's expert, and documentary evidence, conclusively establish that the cleavage agent utilized in Novo's process was well known to those skilled in the art (95 Tr. 1771-1777 Falkinham; 96 Tr. 171 Falkinham; GNE 216, p. 209, GNE 223, p. 243). The court thus finds that the design and use of [Text redacted by Court] and the use of [Text redacted by Court] were enabled by the '199 patent and the state of the art in 1979.

75. Buttressing this point, Dr. Dalboge started at Novo in the [Text redacted by Court] (95 Tr. 549 Dalboge). [Text redacted by Court] Thus, Novo's own work shows that the use of cleavable enzymes was predictable. [Text redacted by Court] Of course, enablement does not require commercial scale production. Thus, the court finds that Novo's process for producing a cleavable fusion expression protein did not require undue experimentation.

76. Novo's final argument is that the Great Britain patent referenced in the '199 patent teaches away from using trypsin and is, therefore, not enabling (96 Tr. 1250-1251, Villa-Komaroff) due to trypsin-cleavable sites inside the hGH protein chain. The court finds this argument untenable in view of the knowledge in the art by 1979, and a mischaracterization of the Great Britain patent. The evidence was unrebutted that by using partial proteolysis and blocking agents, cleavage with trypsin would have been easily controlled by one skilled in the art so as to obtain at least some 1-191 hGH (GNE 219, GNE 220; 96 Tr. 301-303, 307-309, 320-321, Ravetch; 96 Tr. 1198-1199, 1253-1254, 1329, Villa-Komaroff; NN 269). Indeed, the Great Britain patent makes reference to both partial proteolysis (using the terminology "competitive binding") and protecting cleavage sites (GNE 222; 96 Tr. 345-348, Ravetch).

77. Thus, Genentech has established a strong likelihood of success on enablement.

D. The '199 Patent Fulfills The Written Description Requirement of Section 112

78. Whether the '199 patent specification fulfills the written description requirement is a question of fact. *Fiers*, 984 F.2d at 1170. The purpose of this requirement is to assure that at the time of filing the application, the inventor was in possession of his invention. *Id.* The law does not require, however, that the inventor have actually reduced the invention to practice by experiment; it is well settled that the filing of the application is a constructive reduction to practice. *Hybritech*, 802 F.2d at 1374. Rather, the law requires that there is an antecedent basis for the claim in the original disclosure. *Tandon Corp.* v. *U.S. International Trade Commission*, 831 F.2d 1017, 1024 (Fed. Cir. 1987).

79. To consider support one looks to the entire specification. *In re Wright*, 866 F.2d 422, 425 (Fed. Cir. 1989). The specification in this case provides full support for the claim including an explanation of the problem to be solved and the solution provided by the invention. Novo's characterization of the specification as evidencing an "incomplete conception" is erroneous.

80. The '199 patent (GNE 200, col. 3, lines 56-59) explains the scarcity of human growth hormone derived from cadavers. Thereafter, the inventors describe why the prior art did not solve this problem (*Id.* at col. 3, line 65-col. 4, line 8). The summary of the invention then specifies two solutions, one of which is extracellular cleavage of the conjugate protein (*Id.* at col. 4, lines 11-23). As the Federal Circuit has noted, the specification teaches cleavable fusion expression of human growth hormone. *Novo*, 77 F.3d at 1369.

81. In the detailed description of the invention, the applicants describe how the DNA for 1-191 hGH is made (*Id.* at col. 5, line 5-col. 7, line 29) and how additional DNA is joined for cleavable fusion expression (*Id.* at col. 7, line

30-col. 8, line 11). The conjugate is described in two parts -- "the amino acid sequence of the intended product" and "a measure of extraneous but specifically engineered protein" (*see*, FF 31-33). Enzymatic cleavage is specifically cited, an example is given and the language "for example" is used to express that other enzymes and sequences are included (*see*, FF 53 and 72).

82. Thus, the court determines that Genentech has demonstrated a likelihood of success regarding the support and antecedent basis for the claim.

E. Novo's Allegation Of Inequitable Conduct

83. Novo contends that Genentech committed inequitable conduct in procuring the '199 patent by failing to disclose that it was taking contradictory positions in the prosecution of the '199 patent and in litigation relating to the '980 patent. Novo asserts that Genentech represented to this court, the Federal Circuit and the International Trade Commission that in the '980 patent, the phrase "unaccompanied by the leader sequence of human growth hormone or other extraneous protein bound thereto" (hereinafter "unaccompanied . . .") meant that hGH could be expressed without the hGH leader sequence or other uncleavable protein, while Genentech represented to the Patent Office in connection with the '199 patent that the same phrase meant only amino acids 1-191 of hGH.

84. On this motion, Genentech bears the burden of establishing the likelihood of succeeding at trial with regard to the issue of inequitable conduct by demonstrating that no clear and convincing evidence of inequitable conduct has been adduced. *Nutrition 21* v. *United States*, 930 F.2d 867, 869-70 (Fed. Cir. 1991). Genentech can sustain its burden by showing that Novo has failed to adduce clear and convincing evidence either that Genentech made misrepresentations or omissions of material fact, or that Genentech acted with the intent to deceive. *FMC Corp.* v. *Manitowoc Co., Inc.*, 835 F.2d 1411, 1415-1416 (Fed. Cir. 1987).

85. For the reasons explained below, the court finds that Genentech has made this showing and that Novo's claims of inequitable conduct verge on frivolous. Novo introduced no evidence whatsoever that would suggest an intent by Genentech to deceive the Patent Office. For this reason alone, Novo's charge of inequitable conduct is utterly baseless.

86. In addition, the evidence does not support Novo's charge that Genentech made any misrepresentation to the patent office regarding the "unaccompanied . . ." language. To the contrary, it is clear from the prosecution history of the '199 patent that the Examiner was fully aware of Genentech's interpretation of the phrase "unaccompanied . . ." In particular, the Examiner originally rejected the claim of the '199 patent on the ground that the claim would result in "obviousness-type" double patenting in light of Claim 2 of the '980 patent (GNE 201, p. 82; 96 Tr. 383-385, Peet). In issuing this rejection, the Examiner indicated his agreement with Genentech's interpretation of the phrase at issue. The Examiner stated as follows:

> The *claims* in the '980 patent when read in light of the specification (col. 4, lines 1 through 34; and at least col. 7, lines 20 through 31), *recite cleavage of the polypeptide by enzymatic agents.*

(GNE 201, p. 82). Likewise, in a similar rejection, the Examiner stated:

> Although the conflicting claims are not identical, they are not patentably distinct from each other *because the claims in the '980 patent* (read in light of the patent specification [sic] (see at least col. 4, lines 1-34 and col. 7, lines 20-31) *indicate cleavage by enzymatic agents) are to the same method of producing the hGH from a transformed microorganism. . . .*

Thus the Examiner fully understood, and agreed with, Genentech's assertion that the "unaccompanied . . ." phrase at issue meant without uncleavable protein, or else the '980

patent would have been limited to direct expression and the double patenting rejection would not have been made. *See also*, statement of Examiner Tanenholtz (Def.Ex. 140, Office Action dated July 5, 1988 at 4; 96 Tr. 386-388, Peet). Novo cannot possibly establish that Genentech withheld its "litigation" interpretation from the Examiner (or vice versa), much less that the Examiner was somehow misled by Genentech. To the contrary, the Examiner was aware of, and apparently agreed with, the interpretation that Genentech made to this court, the Federal Circuit, and the International Trade Commission.

87. The phrase "unaccompanied . . ." was consistently utilized by Genentech as a negative limitation. *See* FF 40. As in claim 2 of the '980 patent, the language is negative and explains what is not there. However, in Claim 1 of the '199 patent, Genentech added the words "consists essentially of" to the phrase "1-191 hGH" to make clear that in the context of the '199 patent the portion of the conjugate defined by 1-191 hGH was limited to amino acids 1-191 of hGH (96 Tr. 175, Falkinham; 427, 430-431, 516-521, Peet; GNE 201, pp. 177, 199-200, GNE 215).

88. Therefore, Novo's strained argument that using Genentech's interpretation of "unaccompanied . . ." in the '199 patent would allow for *cleavable* protein attached to cleavable protein is misplaced because it disregards the "consists essentially of" language of the claim which was not in the '980 patent. Because of the "consists essentially of" language, it is clear the hGH is only 1-191 hGH. Of course, the claim then continues that additional amino acids are added to create a conjugate.

89. As part of its inequitable conduct defense, Novo argues that Genentech unfairly delayed issuance of the '199 patent to hide the inconsistency of its position and that had Genentech succeeded on the prior Novo appeal, the '199 patent "never would have seen the light of day" (96 Tr. 50). Novo's argument is without evidentiary support. While Genentech did refile its application, it did so to fulfill its duty of candor (96 Tr.

432, Peet). Specifically, Genentech felt it needed to evaluate contention interrogatory responses sent by its adversary in litigation on related patents and the ITC decision (GNE 201 pp. 217-219). Genentech then allowed the claims to issue and in fact paid the issue fee only two weeks after the ITC commission's review of the Administrative Law Judge's decision (GNE 201 pp. 239-247)

90. In fact, when the patent had not issued after a few months, Genentech requested expedition (GNE 201, p. 251). This request was before Novo even received FDA approval (*see, supra*). Genentech's effort completely undermines Novo's contentions.

91. Finally, Genentech's '199 patent issued before Genentech knew whether it would obtain a preliminary injunction on the '980 patent (and before the Federal Circuit reversal). Once the patent issued, its file became public. Therefore, there is no basis to suggest that had Genentech won on the prior appeal, the '199 patent file would have been hidden. Genentech allowed it to be made public and obviously it would be available to Novo long before full trial.

92. Based on the foregoing, Genentech's refiling was proper.

IV. IRREPARABLE HARM

A. The Presumption Of Irreparable Harm

93. A party who makes a clear or strong showing of patent validity and infringement is entitled to a presumption of irreparable harm. *H.H. Robertson Co.* v. *United Steel Deck, Inc.*, 820 F.2d 384, 390 (Fed. Cir. 1987) ("irreparable harm has been presumed when a clear showing has been made of patent validity and infringement . . .") (citation omitted). Because Genentech has proven a strong likelihood of success on the merits, Genentech is entitled to a presumption of irreparable harm.

B. Goodwill

94. The loss of goodwill may constitute irreparable harm because it is impossible to quantify and cannot be adequately rectified by money damages. *Bio-Technology*, 80 F.3d at 1566; *Medco Research Inc.* v. *Fujisawa U.S.A., Inc.*, No. 93 C 2705, No. 93 C 2724, 1994 U.S. Dist. LEXIS 18323 (N.D. Ill. 1994) (entry of another competitor would confuse customers and would diminish goodwill); *CVI/Beta Ventures, Inc.* v. *Custom Optical Frames, Inc.*, 893 F. Supp. 508, 524 (D. Md. 1995) (defendant's market entry would present risk of irreparable harm to the plaintiff's reputation and goodwill).

1. The United States HGH Market

95. The evidence presented at the hearing confirms that Genentech created and developed the market for recombinant hGH in the United States, filling the need created by the scarcity and eventual unavailability of pituitary hGH (95 Tr. 169-170, 185-187, 210-211, Johanson; 96 Tr. 573-574, Johanson).

97. Genentech's market share has declined to approximately 75% (96 Tr. 621, Matlock; 95 Tr. 276-77, Rizzuto) [Text redacted by Court] In about March 1996, Pharmacia, which, like Lilly, is a Genentech licensee, began selling its hGH in the United States (96 Tr. 648, Matlock).

98. Genentech's 1995 sales of hGH were approximately $219 million (GNE 267). Genentech does not sell hGH outside the United States (96 Tr. 847, Barfod). Although Novo does not sell hGH in the United States, its sales of hGH in other countries [Text redacted by Court] in 1995 (96 Tr. 847-48, Barfod).

2. Programs to Create Goodwill

99. Genentech continues to spend substantial sums on the programs like the National Cooperative Growth Study ("NCGS"), its uninsured patient program, a reimbursement program, and other programs involving education for patients

and parents involved in hGH therapy (96 Tr. 626, Matlock; 95 Tr. 274, Rizzuto).

3. The Customer Base For The United States HGH Market

100. There are a relatively small number of physicians who prescribe hGH -- only approximately 700 pediatric endocrinologists -- and they do not always have control over which drug product to prescribe, because managed care organizations ("MCO") health maintenance organizations ("HMO") and hospital pharmacies often dictate which products doctors may use (96 Tr. 621, 623 Matlock; 96 Tr. 867-88, Barfod; 95 Tr. 852, Cohen). For example, the top five HMO's account for approximately [Text redacted by Court] million of Genentech's business (96 Tr. 623-24, Matlock). Approximately [Text redacted by Court] of Genentech's business is paid for by organizations that are characterized as MCO's (96 Tr. 624, Matlock). Although pediatric endocrinologists do not like to switch patients from one hGH product to another (96 Tr. 625-26, Matlock), [Text redacted by Court] For these reasons, the market for hGH is particularly subject to disruption, and goodwill built in that market is uniquely vulnerable.

4. The Reluctance Of Doctors To Switch Patients

101. Genentech introduced a new hGH formulation, Nutropin AQ, in January 1996 (96 Tr. 702, Matlock). Nutropin AQ is a liquid form of Nutropin which does not require reconstitution so that it simplifies the method of administration, which remains complex and involves many steps (96 Tr. 581, 584, Johanson).

102. There are significant differences among hGH products. For example, there are different vial sizes and labels (96 Tr. 583, Johanson; 95 Tr. 849-850, Cohen). Pharmacia manufacturers a so-called "pen system" for administration (96 Tr. 672-73, Matlock). Novo offers a different "pen system" in Europe, but [Text redacted by Court] (96 Tr. 844-845, Barfod; 95 Tr. 692, Christensen). Novo recommends that injections should be made only in the thigh and only in the evening (96

Tr. 582-83, Johanson; Pl. Ex. 27). In contrast, Genentech recommends injection at several other sites and at any time during the day (96 Tr. 582-83, Johanson). Because of such differences, patients who switch from one product to another will require additional instruction from their doctors and/or nurses (96 Tr. 585-86, Johanson; 95 Tr. 191-193, Johanson).

103. The testimony of Dr. Johanson, who was characterized by Novo's expert as a "pioneer" in hGH therapy (95 Tr. 848-849, Cohen), was consistent with that of Novo's President, Ken Capuano, and Novo's economic expert, Dr. Gregory Bell, that doctors in the United States are reluctant to switch patients from one hGH product to another (96 Tr. 1057, 1073, Bell; 95 Tr. 719-720, Capuano). As Novo's expert Dr. Howard testified, consistency is important and improves compliance (96 Tr. 926, Howard). In Dr. Howard's experience, patients have been switched primarily when required by insurance companies, or when the patient was not responding to treatment (96 Tr. 925, 929, Howard).

105. Dr. Howard, Novo's own expert, agreed that if Norditropin were allowed to come on the market now and Novo started to treat patients and was then forced off the market by an court order, product availability would be disrupted and it would cause "frustration" on the part of the nurses and doctors who use the product (96 Tr. 929-930, Howard). Although Dr. Howard believed that this frustration would not be aimed at Genentech, Dr. Howard conceded that this frustration would not arise if Norditropin were not allowed to come on the market at all (96 Tr. 929-930, Howard). Similarly, Novo's expert in the 1995 hearing, Dr. Cohen, conceded that doctors are likely to be resentful if they are forced to switch products (95 Tr. 852-853, Cohen).

106. The court finds, based on the testimony of Dr. Johanson, and on the admissions of Dr. Cohen, Dr. Howard, Dr. Bell and Mr. Capuano, that doctors are very reluctant to switch products, and that it would be a burden on hGH patients and their parents to require them to relearn and be retrained in a new and different process of administration (96

Tr. 585-86, Johanson; 95 Tr. 192, Johanson). Each of the differences between the old and new products could result in errors leading to poor compliance (96 Tr. 586, Johanson).

107. The court further finds that if Novo is allowed to sell its hGH product in the United States and then after two years or more is taken off the market by reason of an injunction, Genentech's goodwill with doctors and patients will be damaged irreparably (96 Tr. 587-89, Johanson; 96 Tr. 651-52, Matlock; 95 Tr. 193, Johanson). Physicians, parents and children will doubtless be aware of Genentech's role in taking Novo's product off the market and resent it. (*Id.*).

C. Irreparable Harm To Independent Operations, Market Share, Customer Base, And Research And Development Programs

108. The Federal Circuit has recognized that infringement may have market effects, such as decreases in market share and revenue, that are not fully compensable in money. *Atlas Powder Co.* v. *Ireco Chemicals*, 773 F.2d 1230, 1233 (Fed. Cir. 1985); *Hybritech Inc.* v. *Abbott Laboratories*, 849 F.2d 1446, 1457 (Fed. Cir. 1988). Decreases in revenue which cause decreases in research and development funding or lost business opportunities may similarly cause irreparable harm. *Maitland Co., Inc.* v. *Terra First, Inc.*, 33 U.S.P.Q. 2d 1882, 1896 (D.S.C. 1994); *Critikon, Inc.* v. *Becton Dickinson Vascular Access, Inc.*, 28 U.S.P.Q. 2d 1362, 1370 (D.Del. 1993).

1. Novo's Likely Revenues And Market Share

109. Novo's estimates of the hGH sales it would make if allowed to enter the hGH market pending trial were inconsistent and at times differed from Novo's public statements. For example:

(a) In 1995, when Novo was trying to minimize its market impact, Novo estimated that after 2 1/2 years of sales, it would have sold a total of only [Text redacted by Court] million of hGH and would have obtained [Text redacted by Court] of the market (Pl. Ex. 33). Yet when Novo's counsel argued for a high bond, he claimed that Novo would lose sales

of [Text redacted by Court] million per month (or [Text redacted by Court] million in a single year) if enjoined (95 Tr. 2015-2016).

(b) In 1995, again to minimize its market impact, Novo estimated that the typical new patient would weigh less than 15 kg. (Pl. Ex. 31). In 1996, Novo conceded that a typical new patient would weigh 20 - 25 kg., but drastically reduced its estimate of the percentage of new patients it would obtain (*compare* Pl. Ex. 32 *with* NN 212, 213). In order to maximize its own alleged losses resulting from the now vacated 1995 injunction, Novo contended that each lost patient has a present value of about [Text redacted by Court] and that the prior injunction caused a loss of patients since June 1995 and will continue for several more years to cause Novo to lose patients (even if allowed to start marketing now), resulting in alleged losses of over [Text redacted by Court] million;

(c) Novo assumes that there are only [Text redacted by Court] new patients per year (96 Tr. 860-61, Barfod). Genentech, which has better access to reliable U.S. data, estimates that the number is between [Text redacted by Court](96 Tr. 620, Matlock; 95 Tr. 286-287, Rizzuto);

(d) Novo assumes that sales to its new patients will average only about [Text redacted by Court] per year, although it concedes that average sales for all patients are about [Text redacted by Court] per year (96 Tr. 796-97, 813-14, Barfod; 95 Tr. 1251, 1279, Kalos; NN 212, 213);

(e) Novo still assumes that *all* new patients use [Text redacted by Court] mg per year of hGH (NN 212), continuing to underestimate the amount of hGH consumed and consequently sold (*compare* NN 212, 213 *with* Pl. Ex. 33; 95 Tr. 1251-1252, Kalos); and

(f) Despite the volatility of the hGH market, [Text redacted by Court]

110. Novo contends that its entry into the U.S. market would have an insignificant impact on Genentech. Yet Novo's economic expert conceded that Novo's sales as a percentage

of Genentech's hGH sales would go from [Text redacted by Court] in 1996 to [Text redacted by Court] by 1998, and would further increase to [Text redacted by Court] by 2001 (96 Tr. 955, 963, Bell). Novo's expert conceded that this would be a significant drop in sales for Genentech (*Id.*).

111. Accepting Novo's projections as true, Novo will not be [Text redacted by Court] (96 Tr. 802-03, Barfod; NN 214). This would appear to be contrary to Novo's announced business strategy of focusing on core business "where Novo Nordisk already holds -- or has potential to build and maintain -- market leadership" (GNE 248 p. 2). Indeed, in 1995, Novo generated the largest profit in the history of the company, and increased its worldwide hGH sales by [Text redacted by Court] while Genentech's sales of hGH declined (96 Tr. 848-49, Barfod; GNE 248, p. 7).

112. In contrast, it is reasonable to assume that Novo will achieve a [Text redacted by Court] market share by the end of 1997, or sales of [Text redacted by Court] million in a [Text redacted by Court] million market, if it is allowed to start marketing now (96 Tr. 643-44, Matlock).

113. Novo argues that the hGH market has changed since June 1995 because of Nutropin AQ and because of Pharmacia (96 Tr. 788-89, Barfod). But Nutropin AQ is being positioned for new patients and existing patients with compliance problems, and is not appropriate for all patients (96 Tr. 584-85; Johanson; 96 Tr. 652-53, 655, Matlock).

114. Similarly, the entry of Pharmacia does not substantially change the market prospects of Novo. Unlike Pharmacia, Novo has long-standing and extensive relationships with the pediatric endocrinologists that purchase its insulin, which it can leverage to market hGH (96 Tr. 649, Matlock; 96 Tr. 1071-72, Bell; 95 Tr. 902-903, Barfod; Defs. Ex. 89). Novo has continued to maintain contact with pediatric endocrinologists and to engage in pre-marketing activities related to hGH (96 Tr. 636-43, Matlock; 96 Tr. 817-35, Barfod; GNE 246, GNE 247).

115. Therefore, despite alleged changes in the market, the Court finds that Novo's entry into the hGH market would have a substantial impact on Genentech's revenues and market share.

2. Impact On Genentech's Research And Development Programs

116. Loss of revenue leading to a decrease in funding for research and development can cause irreparable harm. *Bio-Technology*, 80 F.3d at 1566; *Abbott Labs.*, 849 F.2d at 1456 (lost research funds considered); *American Dental Assoc. Health Found.* v. *Bisco Inc.*, 24 U.S.P.Q.2d 1524, 1530, (N.D. Ill. 1992) ("lost time or effort with respect to research and development due to a present lack of funds cannot be made up later by throwing money at it"); *contra Eli Lilly and Co.* v. *American Cyanamid Co.*, 82 F.3d 1568, 1578 (Fed. Cir. 1996).

117. Since its inception in 1976, Genentech has expended over $2.3 billion dollars in research and development (96 Tr. 737, Whiting), including over $420 million on projects that were terminated before final development (95 Tr. 325, Whiting), and more than $422 million on research and development of hGH products alone (95 Tr. 327, Whiting).

118. Genentech's primary focus -- breakthrough products that meet unmet medical needs -- is inherently riskier and costlier than the development of other products for which treatment exists--so-called "me-too" products (96 Tr. 741, Whiting; 95 Tr. 326, Whiting). Genentech scientists are encouraged to engage in so-called curiosity projects (96 Tr. 742-43, Whiting; 95 Tr. 321-322, Whiting), which have led to the discovery of potential products, the most notable example of which is Pulmozyme (95 Tr. 321-322; Whiting).

119. In 1995, Genentech spent approximately $363 million on research and development, or 40% of its total revenues (96 Tr. 739, Whiting, GNE 266, 267; 95 Tr. 322, Whiting), and it plans to increase research and development spending (GNE 249, p. 30).

120. At Genentech, the level of research and development expenditures has been directly related to revenues and, historically, changes in anticipated revenues have resulted in

121. A decline of [Text redacted by Court] in Genentech's hGH revenues would have a significant impact on the funds available for research (96 Tr. 643-645, Matlock; 748, Whiting). Since timing is critical to research, an opportunity missed because of a lack of funds cannot be recaptured if the funds are made available later in the form of damages (96 Tr. 769-770, Whiting). Moreover, Genentech's funding of things such as curiosity projects, post-doctoral programs and university collaborations makes Genentech's claim of lost funding for research and development distinct from claims that could be made by any company with a research and development program, and distinguishes this case from *Eli Lilly & Co.* As Novo's economic expert testified, in most cases a company can select which projects to continue and which do not make financial sense (96 Tr. 999, Bell). The projects most likely to be cut are those which are the most theoretical -- like "curiosity projects"-- and it is therefore impossible to know what results those projects would have produced.

3. Genentech's Relationship With Roche Holdings

122. Although Roche Holdings currently owns 64% of Genentech's stock, the independent public shareholders of Genentech (i.e., the non-Roche shareholders) retain the power to elect 11 of Genentech's 13 board members, and Genentech continues to operate independently of Roche (96 Tr. 1098-01, Bell; GNE 282, p. 9). Genentech has stated its desire to continue independent operations (96 Tr. 1099, Bell; GNE 249, p. 2).

123. Pursuant to an agreement between Genentech and Roche, Roche has an option to purchase all of the outstanding stock of Genentech not presently owned by Roche at a substantial premium over the present market price of approximately $52 per share (96 Tr. 746-47, Whiting; GNE 249; GNE 282). Roche has the option to purchase the stock at prices which increase quarterly, rising to $82 per share in

1999 (96 Tr. 746-47, Whiting; GNE 249, p. 33; GNE 282, p. i). If Roche does not exercise its option, then the public shareholders have the right, exercisable in 1999, to require Roche to purchase their shares for $60 per share (*Id.*). Thus, if Genentech's stock is trading for less than $60 per share in 1999, the public shareholders will be effectively compelled to sell their shares to Roche, and Genentech will likely cease independent operations (96 Tr. 747, Whiting; 96 Tr. 1006-08, Bell).

124. In order to give public shareholders the opportunity and incentive to opt for continued independent operations by holding on to their shares, Genentech has adopted several new strategic objectives, including increasing research and development spending over the short term in order to move products in development through the "pipeline" to commercial sale as quickly as possible, and to steadily increase earnings prior to 1999 (96 Tr. 747, Whiting). Both of these objectives require that present revenue levels be sustained and increased, which would be frustrated by a decrease in earnings resulting from Novo's premature entry into the market (*Id.*).

125. This court disagrees with Novo that Genentech's liquid assets of approximately $1 billion could be used to fund research and development without causing irreparable harm to Genentech because a decrease in those funds would result in an increase in expense and a resulting decrease in earnings, adversely affecting the share value (96 Tr. 748-49, Whiting). If Novo is allowed to infringe pending trial, and is compelled to pay damages after 1999, there is a substantial possibility that such damages would be paid to a different company than the present Genentech (*Id.*). The harm which Genentech may sustain by being unable to increase earnings and preserve its independent operations cannot be compensated by money damages alone and is akin to cases in which irreparable harm stems from a hostile tender offer, or where lost sales threaten the viability of a business. *See Consolidated Gold Fields PLC* v. *Minorco, S.A.*, 871 F.2d 252, 261 (2d Cir.), *cert. denied*, 492 U.S. 939 (1989) ("once the tender offer has been consummated it becomes difficult, and sometimes virtually

impossible, for a court to 'unscramble the eggs'") (citations omitted); *Petereit* v. *S.B. Thomas, Inc.*, 63 F.3d 1169, 1186 (2d Cir. 1995), *cert. denied*, ___ U.S. ___, 116 S. Ct. 1351 (1996) (lost profits may threaten the viability of plaintiffs' businesses). Accordingly, the court finds that future money damages are an inadequate remedy for infringement.

V. THE BALANCE OF EQUITIES TIPS DECIDEDLY IN GENENTECH'S FAVOR

126. Genentech's pioneering invention and its vast expenditures on research and development created hGH technology and the United States market for hGH. Genentech's '199 patent expires in 2003. By the time this case is finally decided, Genentech will have five years or less of remaining patent protection. *See Robertson*, 820 F.2d at 391 (granting preliminary injunction where patent did not have many years to run); *Sensormatic Electronics Corp.* v. *Minnesota Mining and Manufacturing Co.*, 10 U.S.P.Q.2d 1467, 1470 (S.D. Fla. 1988) (granting preliminary injunction where remaining two years of patent were "critical" to the industry).

127. In contrast, Novo has not yet entered into the United States market and accordingly does not stand to lose goodwill or comparable expenditures from a preliminary injunction maintaining the status quo. As the Federal Circuit has recognized, "[w]hen the movant has shown the likelihood that the acts complained of are unlawful, the preliminary injunction 'preserves the status quo if it prevents future trespass' but does not undertake to assess the pecuniary or other consequences of past trespasses . . ." *Robertson*, 820 F.2d at 390-91 (citation omitted) (affirming grant of preliminary injunction). [Text redacted by Court]

128. Accordingly, the court finds that the balance of equities weigh in favor of Genentech.

VI. THE PUBLIC INTEREST FAVORS THE GRANTING OF A PRELIMINARY INJUNCTION

129. The Federal Circuit has held that public interest favors the grant of injunctions, including preliminary

injunctions, to stop patent infringement. *Smith International, Inc.* v. *Hughes Tool Co.*, 718 F.2d 1573, 1578 (Fed. Cir. 1983) ("Without the right to obtain an injunction, the right to exclude granted to the patentee would have only a fraction of the value it was intended to have and would no longer be as great an incentive to engage in the toils of scientific and technological research"), *cert. denied*, 464 U.S. 996 (1983). Indeed, the "protection of patents furthers a strong public policy . . . advanced by granting preliminary injunctive relief when it appears that, absent such relief, patent rights will be flagrantly violated." *Robertson*, 820 F.2d at 391. Moreover, patent grants inspire researchers to explore, at their own risk and expense, uncharted territory in the quest for knowledge. *See Eli Lilly and Co.* v. *Premo Pharmaceutical Labs.*, 630 F.2d 120, 137 (3d Cir.), *cert. denied*, 449 U.S. 1014 (1980); *Ortho Pharmaceutical Corp.* v. *Smith*, 18 U.S.P.Q. 2d 1977, 1989 (E.D.Pa. 1990), *aff'd*, 959 F.2d 936 (Fed. Cir. 1992) ("[t]he policy rationales behind the patent statutes generally apply with even greater strength in the case of drug patents. It is in the public interest to protect the pharmaceutical industry's investment into the discovery of new drugs"). Novo's own policy statement on biotechnology patents concedes that because this industry involves high inventive costs and low production costs, it is sensitive to copying and piracy, making patents essential (GNE 276).

130. In addition, it is in the public interest to minimize disruption in customers' product usage with the issuance of a preliminary injunction which precludes long-term utilization of and reliance on an allegedly infringing product. *Critikon*, 28 U.S.P.Q. 2d at 1371.

VII. CONCLUSION

Genentech has demonstrated a likelihood of success on the merits of its infringement claim and has shown that it will suffer irreparable injury in the absence of a preliminary injunction. Accordingly, Genentech's motion for a preliminary injunction is granted and Novo's motion to dismiss Genentech's complaint is denied.

Dated: June 26, 1996
New York, New York

/s/ Constance Baker Motley

CONSTANCE BAKER MOTLEY
United States District Judge

APPENDIX C

Appendix C

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

ORDER

A combined petition for rehearing and suggestion for rehearing in banc having been filed by the APPELLEE, and a response thereto having been invited by the court and filed by the APPELLANT, and the petition for rehearing having been referred to the panel that heard the appeal, and thereafter the suggestion for rehearing in banc and response having been referred to the circuit judges who are in regular active service,

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for rehearing be, and the same hereby is, DENIED and it is further

ORDERED that the suggestion for rehearing in banc be, and the same hereby is, DECLINED.

The mandate of the court will issue on May 19, 1997.

FOR THE COURT,
JAN HORBALY, CLERK

Dated: May 12, 1997

By /s/ Brian LeDuc
Brian P. LeDuc
Associate Chief Deputy Clerk

cc: ALBERT L. JACOBS
LEORA BEN-AMI

FILED
U.S. COURT OF APPEALS
FOR THE FEDERAL CIRCUIT
MAY 12 1997
JAN HORBALY
CLERK

GENENTECH INC V NOVO NORDISK A/S, 96-1440 (DCT - 95-CV-3474)

Note: Pursuant to Fed. Cir. R. 47.6, this order is not citable as precedent. It is a public record.